Chapter 20

MEDICAL MANAGEMENT OF POTENTIAL BIOLOGICAL CASUALTIES: A STEPWISE APPROACH

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INTRODUCTION

If the identity of an agent used in a biological attack is known, response to such an attack is, in some sense, relatively straightforward. Earlier chapters in this volume deal with diagnoses and treatment strategies specific to known infectious and toxic agents. A larger problem arises, however, when the identity of an agent is uncertain. In some cases, a biological attack might be threatened or suspected, but it may remain unclear if such an attack has actually occurred. Moreover, it may be unclear whether casualties in certain situations arise from exposure to a biological, chemical, or radiological agent; result from a naturally occurring infectious disease process or toxic industrial exposure; or simply reflect a heightened awareness of background disease within a community or population. Recent experiences with West Nile virus,[1] severe acute respiratory syndrome,[2] pneumonic tularemia,[3,4] and monkeypox[5] highlight this dilemma. In each case, the possibility of bioterrorism was raised, although each outbreak was ultimately proven to have had an inocuous origin. In some instances, proof of such origins can be difficult or impossible to obtain, thus providing plausible deniability—or the precise reason some bioterrorists choose specific biological agents. This chapter provides a structured framework for dealing with outbreaks of unknown origin and etiology on the battlefield, as well as in a potential bioterrorism scenario involving military support installations or the civilian population.

A 10-STEP APPROACH TO CASUALTY MANAGEMENT

In responding to the unknown, it is helpful, in many situations, to use a standardized, stepwise approach. This would be especially true with a medical mass casualty event, in which the use of such an approach (as advocated by the Advanced Trauma Life Support model sponsored by the American College of Surgeons[6]) is already well accepted and practiced. This stepwise approach would also be helpful under austere or battlefield conditions. Although major theater-level (level 4) and continental United States-based (level 5) military medical centers (and research institutions such as the US Army Medical Research Institute of Infectious Diseases [USAMRIID]) and the US Army Medical Research Institute of Chemical Defense may possess sophisticated diagnostic and response capabilities, the medical provider on the battlefield and at lower level medical treatment facilities is typically required to make rapid, therapeutic decisions based on incomplete information and with little immediate support. Civilian clinicians, first responders, and public health personnel who practice in rural or remote areas during a terrorist attack would face similar decision-making challenges. In the setting of a biological (or chemical or radiological) attack, similar to the setting of a medical mass casualty trauma event, these decisions may have life-and-death implications. In these situations, a stepwise or algorithmic approach becomes invaluable.

USAMRIID has developed a 10-step approach to the management of casualties that might result from biological warfare or terrorism:

1. Maintain a healthy index of suspicion.
2. Protect yourself.
3. Save the patient's life (the primary assessment).
4. Disinfect or decontaminate as appropriate.
5. Establish a diagnosis (the secondary assessment).
6. Provide prompt therapy.
7. Institute proper infection control measures.
8. Alert the proper authorities.
9. Conduct an epidemiological investigation and manage the psychological aftermath of a biological attack.
10. Maintain a level of proficiency.

Many facets of this approach could also be helpful in dealing with potential chemical or radiological casualties. It is no longer adequate for clinicians and medical personnel simply to understand disease processes. Rather, these personnel (whether military or civilian) must have tactical, operational, and strategic knowledge of threat response (and knowledge of disaster response in general) as it applies to weapons of mass destruction:

- Tactical response concerns those elements of diagnosis and treatment of specific diseases that have traditionally been the realm of the individual clinician.
- Operational response involves the mechanisms by which the provider interacts with his or her institution (eg, hospital, clinic, medical unit) to provide mass care during a disaster.
- Strategic response involves systemwide disaster preparedness and response. In a civilian setting, the response would include mechanisms by which state and federal disaster response elements might become involved.

Currently, medical personnel need to have at least a basic understanding of operational and strategic response, in addition to a firm grounding in tactical medical and public health intervention.

In the 10-step USAMRIID approach, steps 1 to 7 deal predominately with tactical response (ie, at the level of the individual provider). Steps 8 and 9 transition into operational and strategic response (ie, at the level of the institution and the system as a whole). Derivation of this 10-step approach is reported elsewhere,[7–10] and a condensed version of it appears in recent editions of USAMRIID's *Medical Management of Biological Casualties Handbook* (or the *Blue Book*).[11] The following is an overview of this stepwise approach.

Step 1: Maintain a Healthy Index of Suspicion

In the case of chemical warfare (or terrorism), the intentional nature of an attack is often evident. Most likely, victims would be tightly clustered in time and space (ie, they would succumb in close proximity—both temporally and geographically—to a dispersal device). Complicating discovery of the intentional nature of a biological attack, however, is the fact that biological agents possess inherent incubation periods, whereas conventional, chemical, and nuclear weapons do not. These incubation periods, typically lasting several days (but up to several weeks as with *Coxiella burnetii* and *Brucellae*), allow for the wide dispersion of victims in time and space. Additionally, incubation periods make it likely that the first responders to a biological attack would not be firemen, policemen, paramedics, or other traditional first responders, but rather primary care providers, hospital emergency departments, and public health officials. In these circumstances, maintenance of a healthy index of suspicion is imperative.

In some instances, maintaining an index of suspicion might be easy because patients with diseases caused by biological agents may present with specific characteristic clinical findings, which result in a very limited differential diagnosis. The hallmark presentation of inhalational anthrax is a widened mediastinum, a clinical finding seen in few naturally occurring conditions. In botulism, the hallmark presentation is a descending, symmetric, flaccid paralysis. Whereas an individual patient with flaccid paralysis might prompt consideration of disorders such as Guillain-Barre syndrome, Eaton-Lambert syndrome, poliomyelitis, and myasthenia gravis, the near-simultaneous presentation of multiple patients with flaccid paralysis should quickly prompt consideration of a diagnosis of botulism. Similarly, persons with plague often exhibit hemoptysis in the later stages of illness. Such a finding is uncommon among previously healthy individuals, but it can be caused by tuberculosis, staphylococcal and *Klebsiella* pneumonia, carcinoma, and trauma. Multiple patients with hemoptysis, however, should prompt consideration of a diagnosis of plague. Smallpox is characterized by a unique exanthem, perhaps like *Varicella* or syphilis in its earliest stages, but readily distinguishable from these entities as it progresses.

Yet, by the time each of these characteristic findings develops, treatment is likely to be ineffective. Therefore, therapy is best instituted during the incubation or prodromal phases of these diseases if it is to be beneficial. Unfortunately, however, in their prodromal forms these diseases are likely to appear as simple, undifferentiated febrile illnesses, difficult (if not impossible) to distinguish from other common infectious diseases. Similarly, many other diseases potentially arising from a biological attack (eg, tularemia, brucellosis, melioidosis, Q fever, staphylococcal enterotoxin intoxication, and Venezuelan equine encephalitis) appear simply as undifferentiated febrile illnesses throughout their disease course. Prompt diagnosis and institution of targeted therapy are possible only with the maintenance of a very high index of suspicion.

Epidemiological clues can lead the clinician to suspect that a disease outbreak may have been intentional.[12] Large numbers of persons tightly clustered in time and space, or limited to a discrete population, should raise suspicion. Similarly, unexpected deaths and cases of unexpectedly severe illness merit concern. An outbreak of a disease not typically seen in a specific geographic location, in a given age group, or during a certain season warrants further investigation. Simultaneous outbreaks of a disease in noncontiguous areas should prompt consideration of an intentional release, as should simultaneous or sequential outbreaks of different diseases in the same locale. Even single cases of uncommon illness, such as anthrax or certain viral hemorrhagic fevers (Ebola, Marburg, Lassa, etc), would be suspicious, and a single case of smallpox would almost certainly represent an intentional release. The presence of dying animals (or the simultaneous occurrence of zoonotic disease outbreaks among humans and animals) might provide evidence of an unintentional aerosol release. Evidence of a disparate attack rate between individuals known to be indoors and outdoors at a given time should also be sought out and evaluated. Intelligence reports, terrorist claims, and the discovery of aerosol spray devices would lend credence to the theory that a disease outbreak was of sinister origin. The epidemiological clues to a bioterrorist attack are summarized in Exhibit 20-1.

On the modern battlefield, an array of developing technology is increasingly available to assist clinicians, preventive medicine and chemical corps personnel, operators, and commanders in maintaining their index of suspicion through early, stand-off detection of biological threats. The Portal Shield Biological Warfare Agent

EXHIBIT 20-1

EPIDEMIOLOGICAL CLUES TO A BIOTERRORIST ATTACK

- Presence of an unusually large epidemic.
- High infection rate.
- Disease limited to a discrete population.
- Unexpected severity of disease.
- Evidence of an unusual route of exposure.
- Disease in an atypical geographic locale.
- Disease occurring outside normal transmission seasons.
- Disease occurring in the absence of usual vector.
- Simultaneous outbreaks of multiple diseases.
- Simultaneous occurrence of human and zoonotic disease.
- Unusual organism strains.
- Unusual antimicrobial sensitivity patterns.
- Disparity in attack rates among persons indoors and outdoors.
- Terrorist claims.
- Intelligence reports.
- Discovery of unusual munitions.

Data source: Pavlin JA. Epidemiology of bioterrorism. *Emerg Infect Dis*. 1999;5:528–530.

Detection System (Bio-Rad Laboratories, Hercules, Calif) is the first automated biological detection system of the US Department of Defense. It was designed to provide fixed-site protection to air and port facilities. The Portal Shield is equipped with modular sensors capable of simultaneously assaying for eight different threat agents and providing presumptive identification within about 25 minutes. The Biological Integrated Detection System (BIDS; Battelle, Columbus, Ohio) is a high-mobility, multipurpose, wheeled, vehicle-mounted system (Figure 20-1) equipped with samplers, an aerodynamic particle sizer, a flow cytometer, a chemical-biological mass spectrometer, and other sophisticated assays to permit rapid, real-time detection of multiple biological threat agents on the battlefield. BIDS was first fielded as a single company of 38 units in 1996; current plans call for a dramatic expansion of BIDS capabilities, with 17 companies planned by the end of 2009. The Joint Biological Point Detection System (Battelle, Columbus, Ohio) is the next-generation successor to the BIDS and is envisioned as integrating into the BIDS platform. Purportedly, the Joint Biological Point Detection System will be capable of definitively identifying biowarfare threat agents within 15 minutes. Until such technology is refined, validated, and made widely available, clinicians, health officials, chemical personnel, and commanders must rely on clinical, epidemiological, and intelligence clues to maintain their index of suspicion.

Step 2: Protect Yourself

Providers who become casualties themselves are of little use to their patients. Before approaching casualties of biological or chemical warfare or victims of a terrorist attack, clinicians should be familiar with the basic means of self-protection. Generally, these protective measures fall into one of three categories: (1) physical protection, (2) chemical protection, and (3) immunological protection. Under a given set of circumstances, clinicians might appropriately avail themselves of one or more of these forms of protection.

Physical Protection

Since the beginning of modern gas warfare on the battlefields near Ypres, Belgium, in 1915, physical protection during military operations has involved gas masks and, more recently, charcoal-filled chemical protective overgarments. Although military-style protective clothing and masks were designed with chemical agent protection in mind, they are also capable of offering protection against biological agents. Even though some have advocated the issuance of military-style protective masks and ensembles to civilians (eg, the Israeli government has issued masks to its general populace), such items—even if offered—would probably be unavailable to civilians at the precise moment a threatening agent is released. The unannounced release of colorless and odorless biological agents by terrorists

Fig. 20-1. The Biological Integrated Detection System (BIDS) is a semi-automated biological agent detection/identification suite mounted on a dedicated heavy high mobility multipurpose wheeled vehicle. The system uses multicomplimentary bio-detection technologies.

would afford people no opportunity to don such protective gear, even if it was available. The misuse of protective equipment in the past has led to fatalities, including the suffocation of infants and adults in protective ensembles.[13,14] Although military chemical-biological masks—such as the M40/42 series (ILC Dover LP, Frederica, Del), the M45 series (ILC Dover LP, Frederica, Del), the M43/48 series (for aviators; ILC Dover LP, Frederica, Del), and the next-generation XM50 series (known as the JSGPM or the Joint Service General Purpose Mask; Avon Rubber plc, Melksham, Wiltshire, UK)—provide ample protection against inhalation hazards posed by chemical and biological weapons, as well as radioactive dust particles, they are potentially mission degrading and are unnecessary if and when the threat is limited to biological agents. A simple surgical mask will protect against inhalation of infectious aerosols of virtually any of the biological agents typically described in a terrorism context. The lone exception might be smallpox, in which case a high-efficiency particulate air (HEPA) filter mask would be ideal. With the exception of smallpox, pneumonic plague, and certain viral hemorrhagic fevers, agents in the Centers for Disease Control and Prevention (CDC) categories A and B (Table 20-1) are not contagious by the respiratory route. Thus, respiratory tract protection is necessary when operating in an area of primary release, but would not be required in most patient-care settings (see step 7).

Chemical Protection

During Operations Desert Shield/Storm, tens of thousands of US troops were given pyridostigmine under an emergency use authorization. In early 2003 the US Food and Drug Administration (FDA) gave its final approval for use of pyridostigmine bromide as a "preexposure" means of prophylaxis against intoxication with soman, an organophosphate-based chemical nerve agent. Similar strategies might be used against biological weapons. For example, if a specific terrorist group possessing a specific weaponized agent was known to be operating in a given locale, public health authorities might contemplate the widespread distribution of an appropriate prophylactic antibiotic. Opportunities to implement such a strategy, however, remain limited.

Immunological Protection

For the near future, active immunization may offer one of the most practical methods for providing preexposure prophylaxis against biological attack. In the military, decisions about vaccination are made at the highest levels of policy making, typically through the office of the assistant secretary of defense for health affairs, with input from high-level military medical, public health, and intelligence sources. The decision to offer a specific vaccine in a particular circumstance is a

TABLE 20-1

CRITICAL AGENTS FOR HEALTH PREPAREDNESS

Category A*	Category B†	Category C‡
Variola virus	*Coxiella burnetii*	Nipah virus
Bacillus anthracis	*Brucellae*	Hantaviruses
Yersinia pestis	*Burkholderia mallei*	Yellow fever virus
Botulinum toxin	*Burkholderia pseudomallei*	Drug-resistant tuberculosis
Francisella tularensis	Alphaviruses	Tick-borne encephalitis
Filoviruses and arenaviruses	Certain toxins (ricin, staphylococcal enterotoxin B, trichothecenes)	
	Food safety threat agents (Salmonellae, *Escherichia coli* O157:H7)	
	Water safety threat agents (*Vibrio cholerae*)	

*Agents with high public health impact requiring intensive public health preparedness and intervention.
†Agents with a lesser need for public health preparedness.
‡Other biological agents that may emerge as future threats to public health.
Adapted from Centers for Disease Control and Prevention. Biological and chemical terrorism: strategic plan for preparedness and response. Recommendations of the CDC Strategic Planning Workgroup. *MMWR Recomm Rep*. 2000;49(RR-4):1–14.

complex one that must include a careful risk–benefit calculation. During Operations Desert Shield/Storm, about 150,000 service members received at least one dose of anthrax vaccine, and about 8,000 service members received botulinum toxoid. Since 1998 the US military has intermittently used force-wide anthrax vaccination, and since 2003 the US military has administered smallpox vaccine to deploying troops and certain medical response teams.

In a civilian counterterrorism context, the decision to use a specific vaccine is perhaps even more complex. Factors that would influence a decision by public health officials to recommend vaccination include the following:

- Intelligence
  - How likely and/or plausible is an attack?
  - How imminent is the threat?
  - How specific is the threat?
- Vaccine safety
- Vaccine availability
- Disease consequences
  - Is the threat from a lethal agent?
  - Is the threat from an incapacitant?
- Availability of postexposure prophylaxis and/or therapy

Recently, civilian public health and policy planners have considered the widespread distribution of anthrax and smallpox vaccines.

Anthrax. Anthrax vaccine adsorbed (AVA [BioThrax]; BioPort Corporation, Lansing, Mich) is a fully licensed product approved by the FDA in 1970. The vaccine consists of a purified preparation of protective antigen, a potent immunogen necessary for entry of key anthrax toxin components (lethal and edema factors) into mammalian cells. Administered alone, protective antigen is nontoxic. In a large controlled trial, AVA was effective in preventing cutaneous anthrax among textile workers.[15] Based on an increasing amount of animal data, this vaccine likely is also effective in preventing inhalational anthrax.[16] At least 20 clinical studies, surveys, and reports demonstrate the safety of AVA,[17,18] and the FDA recently reaffirmed the vaccine as safe and effective.[19] Whereas widespread usage of AVA has occurred within the US military (as of September 2005, more than 5.2 million doses of AVA had been given to more than 1.3 million service members), logistical and other considerations make large-scale civilian employment impractical at present. The vaccine is licensed as a six-dose series, given at 0, 2, and 4 weeks, and at 6, 12, and 18 months. Yearly boosters are recommended for those with ongoing risk of exposure. The FDA approves AVA only for persons between the ages of 18 to 65, further complicating any potential civilian anthrax vaccination strategy. Although a large-scale preexposure offering of AVA to the general public might be problematic, some experts recommend that three doses of the vaccine, given simultaneously with antibiotics, may enhance protection and/or enable the clinician to shorten a postexposure antibiotic course.[20] According to some experts, a three-dose series of AVA (given at time 0 and at 2 and 4 weeks after the initial dose)—combined with 30 days of antibiotics—might be an acceptable alternative to longer (60–100-day) antibiotic courses alone in the treatment of, or postexposure prophylaxis against, inhalational anthrax. Currently, no human studies exist to support such a strategy, and AVA is not licensed by the FDA for postexposure prophylaxis or therapy.

Smallpox. Widespread vaccination against smallpox is equally controversial and problematic. In December 2002, a plan to vaccinate selected US healthcare workers and military personnel was announced. Within the Department of Defense, service members deploying to locations believed at risk for biological attack and members of designated smallpox epidemiological and clinical response teams were selected for vaccination. As of September 30, 2005, 875,890 military response team members, hospital workers, and operational forces had been vaccinated, with one death that occurred from a lupus-like illness. Although the emergence of myopericarditis (there were 102 confirmed, suspected, or probable cases among the vaccinees) as a complication of vaccination[21] led to a revision of prevaccine screening (candidates with multiple cardiac risk factors are now excluded), rates of other adverse reactions were low. No cases of eczema vaccinatum, fetal vaccinia, or progressive vaccinia occurred. Only 84 cases of autoinoculation and 54 instances of transfer of vaccinia to family members and other intimate contacts occurred.[22] Vaccinia immune globulin was required on only three occasions: to treat two patients with ocular vaccinia[23] and to treat a burn patient with a recent immunization. The success of this program suggests that mass vaccination can be accomplished with greater safety than previously believed.[24]

Whereas universal civilian vaccination was not recommended under the vaccination plan, the possibility of a future strategy calling for such recommendations arose, and provisions were made to provide smallpox vaccine to members of the general public who specifically requested it. The risk–benefit analysis of this widespread civilian vaccination is difficult to assess. Risks of smallpox vaccination are well known and can be significant.[25,26] The benefits of a civilian vaccination program, however, are less well determined; although

the global eradication of smallpox is one of the greatest public health accomplishments—and the wisdom of administering vaccination with live vaccines remained unquestioned during the era of endemic smallpox—the likelihood of contracting smallpox today via a terrorist attack is unknown. Thus, the risk–benefit calculation in this scenario is not based solely on medical considerations, but also on intelligence estimates.

Despite these concerns, a prerelease mass vaccination program for the general population may be the most effective countermeasure to the terror threat posed by smallpox. By inducing individual and herd immunity, and by obviating the extreme difficulty of conducting postrelease vaccine and quarantine programs, a program involving the resumption of universal smallpox vaccination possesses distinct advantages over other response plans. However, such an approach is hampered not only by the unknown risk of a smallpox release, but also by vaccine supply, safety, and logistics issues.[27,28]

A large number of persons are at risk for severe vaccine reactions today, compared with the previous era of routine civilian smallpox vaccination, which ended in 1972. This increase in risk is due to an estimated 10 million persons in the United States who have compromised immunity associated with the human immunodeficiency virus, the advances in immunosuppressive therapy, and bone marrow and solid organ transplantation. This phenomenon raises concern about the safety and risk–benefit ratio of any preexposure vaccination program.[29] Similarly, the occurrence of rare but severe smallpox vaccine complications in otherwise healthy recipients could result in morbidity and mortality that would be unacceptable in times of low risk. Risk analysis favors prerelease mass vaccination of the general population if the probability of a large-scale attack is high. Prerelease mass vaccination of healthcare workers, however, could be considered in the setting of lower attack probability because of the risk of exposure while caring for patients and the benefit of keeping healthcare workers healthy and functioning in an epidemic setting.[30]

The smallpox vaccine used in the United States is Dryvax (Wyeth Laboratories, Marietta, Pa), a preparation derived from the harvested lymph of calves inoculated with a strain of vaccinia virus, an orthopoxvirus closely related to the variola virus. Production of Dryvax ceased in 1981, and lots in use are at least 25 years old. A new cell-culture derived vaccinia has been licensed by the FDA (September 2007); 300 million doses have been stockpiled by the US Department of Health and Human Services for emergency use. This vaccine is relatively easy to mass produce. These new vaccines are produced in cell culture rather than in calf lymph. It is unlikely that this will significantly diminish the risk of adverse reactions, however, because the new vaccines will use the same live strain of vaccinia virus. The majority of adverse reactions to current vaccinia virus-containing vaccines are derived from the live nature of the virus rather than the method of preparation. To minimize the risks to immunocompromised vaccine recipients, the US Department of Health and Human Services awarded a contract to add 20 million doses of a highly attenuated smallpox vaccine, modified vaccinia Ankara, to the national biodefense stockpile. This vaccine is undergoing completion of phase II clinical trials in both healthy and immunocompromised subjects.

Release of civilian Dryvax stocks is controlled by the CDC, and conditions for such release have been established.[31] The current CDC smallpox response strategy is based on preexposure vaccination of carefully screened first responders and members of epidemiological and clinical response teams. The CDC plans also provide for a program to treat certain severe complications of vaccination using vaccinia immune globulin under an investigational new drug protocol, as well as for compensation of people experiencing such complications through the Smallpox Vaccine Injury Compensation Program (US Department of Health and Human Services, Health Resources and Services Administration, Merrifield, Va).[32]

The CDC response plan calls for ring vaccination after a smallpox release: identification and isolation of cases, with vaccination and active surveillance of contacts. Mass vaccination would be reserved for instances in which the number of cases or the location of cases renders the ring strategy inefficient, or if the risk of additional smallpox releases is high.[33] Although ring vaccination was successful historically (in the setting of herd immunity), mathematical models predict that this strategy may be problematic when applied to large or multifocal epidemics.[34] Controversy exists among experts regarding the predicted benefit of postrelease mass vaccination from the lack of herd immunity, a highly mobile population, a relatively long incubation period, and the difficulties associated with prompt implementation of quarantine and mass vaccination.[35,36] Vaccination is one component of a multifaceted response, which should also include the following:

- farsighted planning and logistical preparation,
- risk communication,
- surveillance,
- treatment,
- isolation, and
- quarantine.

Other agents. Few authorities, either military or civilian, have advocated widespread vaccination against potential agents of bioterrorism other than anthrax and smallpox. Implementation of any such strategy would be problematic. A vaccine against plague, previously licensed in the United States, is no longer produced. This vaccine, which required a three-dose primary series that was followed by annual boosters, was licensed only for persons 18 to 61 years old. Although reasonably effective against bubonic plague and widely used by the Department of Defense to protect against endemic disease, the vaccine probably afforded little protection against pneumonic plague, the form of disease likely to be associated with warfare or terrorism. A vaccine against one specific viral hemorrhagic fever (yellow fever) is widely available, although its causative virus is not regarded as a significant weaponization threat by most policy makers and health officials. The US military administered yellow fever vaccine to large numbers of troops to guard against endemic disease rather than a bioweapons threat. Additionally, a vaccine against Q fever (Q-Vax; [*C burnetii* vaccine; CSL Limited, Victoria, Australia]) is licensed in Australia. Although this vaccine might be a useful addition to the military biodefense armamentarium, the self-limited nature of Q fever makes it unlikely that widespread use of the vaccine would be contemplated for the general public. Numerous research efforts are aimed at developing improved next-generation vaccines against anthrax, smallpox, and plague. Similarly, vaccines effective against tularemia, brucellosis, botulism, equine encephalitides, staphylococcal enterotoxins, ricin, viral hemorrhagic fevers, and other potential agents of bioterrorism are in various stages of development.[37] Investigational vaccines against tularemia, botulism, equine encephalitides (especially Venezuelan equine encephalitis), staphylococcal enterotoxin B, Q fever, and other agents have been used under investigational new drug protocols to protect USAMRIID scientists who study these agents.

Step 3: Save the Patient's Life (the Primary Assessment)

Once self-protective measures are implemented, the clinician can approach the medical mass casualty event scenario and begin assessing patients (also known as the Primary Survey according to Advanced Trauma Life Support guidelines). This initial assessment is brief and limited to the discovery and treatment of those conditions presenting an immediate threat to life or limb. Biological (or chemical) warfare victims may also have conventional injuries. At this point, attention should therefore be focused on maintaining a patent airway and providing for adequate breathing and circulation. The need for decontamination and for the administration of antidotes for rapid-acting chemical agents (eg, nerve agents and cyanide) should be determined at this time. An "ABCDE" algorithm aids the clinician in recalling the specifics of the primary assessment:

A Airway—which should be examined for the presence of conventional injury, but should also be examined because exposure to certain chemical agents (eg, mustard, Lewisite, or phosgene) can damage the airway.
B Breathing—many agents of biological (and chemical) terrorism may cause the patient to experience respiratory difficulty (eg, anthrax, plague, tularemia, botulism, Q fever, staphylococcal enterotoxins, ricin, cyanide, nerve agents, and phosgene).
C Circulation—which may be compromised because of conventional or traumatic injuries sustained during a medical mass casualty event, but may also be involved in septic shock associated with plague and in circulatory collapse associated with viral hemorrhagic fevers.
D Disability—specifically, neuromuscular disability; note that botulism and nerve agent exposures are likely to present with a preponderance of neuromuscular symptomatology.
E Exposure—In a medical mass casualty event setting, this serves as a reminder to remove the victim's clothing to perform a more thorough secondary assessment. At this point, the need for decontamination and disinfection is considered.

Step 4: Disinfect or Decontaminate as Appropriate

Once patients have been stabilized, decontamination can be accomplished where appropriate. On the battlefield, considerable mature military doctrine drives decontamination efforts that are performed by unit personnel (guided or assisted by specific, highly trained Chemical Corps decontamination companies). However, decontamination, in the classical sense, may not be necessary after a biological attack (the same is not always true after a chemical attack) because of the inherent incubation periods of biological agents. Although patients will not typically become symptomatic until several days after exposure, they are likely to have bathed and changed clothing several times before presenting for medical care, thus effectively accomplishing self-decontamination. Exceptions might include persons directly exposed to an observed attack or persons encountering a substance in a threatening

letter, when common sense might dictate topical disinfection. Even in these situations, bathing with soap and water and using conventional laundry measures would be adequate. Situations such as the threatening letter represent crime scenes. Any medical interest in disinfection must be weighed against law enforcement concerns regarding preservation of vital evidence, which can be destroyed through hasty and ill-considered attempts at decontamination. In the past, significant psychological stress has been caused by unnecessary, costly, and resource-intensive attempts at decontamination.[38] Some of these attempts have involved forced disrobing and showering in public streets, under the prurient eye of media cameras. These problems may be avoided by measured responses to the following[39]:

- announced threat (or presumed hoax),
- telephoned threat and/or the empty letter,
- suspicious package, and
- the delivery device.

The Announced Threat (or Presumed Hoax)

The need to preserve evidence and maintain a chain-of-custody when handling that evidence is an important consideration at any crime scene. Whereas human and environmental health protection concerns take precedence over law enforcement procedures, threat and hoax scenarios require early involvement of law enforcement personnel and a respect for the need to maintain an uncompromised crime scene. Typically, decontamination or disinfection is not necessary.

The Telephoned Threat and/or the Empty Letter

In the majority of cases involving a telephoned threat, no delivery device or package is located. If a device is found and/or a threat is subsequently deemed credible, public health authorities should contact potentially exposed individuals, obtain appropriate information, and consider instituting prophylaxis or therapy. An envelope containing only a written threat poses little risk and should be handled in the same manner as a telephoned threat. Because the envelope constitutes evidence in a crime, however, further handling should be left to law enforcement professionals. In these cases, no decontamination is typically necessary pending results of legal and public health investigations.

The Suspicious Package

When a package is discovered and found to contain powder, liquid, or other physical material, response should be individualized. However, in most cases,

- the package should not be disturbed further,
- the room should be vacated,
- additional untrained persons should be prohibited from approaching the scene and from handling the package or its contents, and
- law enforcement and public health officials should be promptly notified.

People who have come into contact with the contents should remove clothing as soon as practical and seal these items in a plastic bag. Persons should then wash with soap and water[40] and, in most cases, may be sent home after receiving adequate instructions for follow-up and providing contact information. In most cases, antibiotic prophylaxis would not be necessary before the preliminary identification of package contents by a competent laboratory, although decisions to provide or withhold postexposure prophylaxis are best made after consultation with public health authorities. Floors, walls, and furniture would not require decontamination before laboratory analysis is completed. Nonporous contaminated personal items (eg, eyeglasses, jewelry) may be washed with soap and water or immersed in 0.5% hypochlorite (household bleach diluted 10-fold) if a foreign substance has come in contact with the items.

The Delivery Device

If an aerosol delivery device or other evidence of a credible aerosol threat is discovered, the room (and potentially the building) should be evacuated. Law enforcement and public health personnel should be notified immediately and further handling of the device left to personnel with highly specialized training, such as the

- US Army's 22nd Chemical Battalion (also known as the Technical Escort Unit; Aberdeen Proving Ground, Md),
- US Marine Corps' Chemical-Biological Incident Response Force (Camp Lejeune, NC), or
- Federal Bureau of Investigation's Hazardous Materials Response Unit (Washington, DC).

Contact information should be obtained from potential victims and detailed instructions provided. Clothing removal, soap and water showering, and decontamination of personal effects should be accomplished as described previously (the Chemical-Biological Incident Response Force has its own extensive decontamination capabilities). Decisions regarding institution of empirical postexposure prophylaxis pending determination of the nature of the threat and identification of the involved biological agents should be left to local and state public health authorities. In providing a reasoned

and measured response to each situation, public health and law enforcement personnel can minimize the disruption and cost associated with large-scale decontamination, costly hazardous material unit involvement, and the broad institution of therapeutic interventions. These professionals can help avoid widespread public panic.

Step 5: Establish a Diagnosis (the Secondary Assessment)

Once decontamination has been considered and accomplished if warranted, the clinician may perform a more thorough and targeted assessment aimed at establishing a diagnosis (also known as the Secondary Survey according to Advanced Trauma Life Support guidelines). The thoroughness and accuracy used to establish this diagnosis will vary depending on the circumstances of the clinician. At robust levels of care (levels 4 and 5), the clinician may have access to infectious disease and microbiology professionals, as well as to sophisticated diagnostic assays. Under these circumstances, it may be possible to formulate a definitive microbiological diagnosis promptly. However, it is equally conceivable that a primary care provider practicing at lower levels of care (levels 1–3) or in more austere circumstances may need to intervene promptly based on limited information and without immediate access to subspecialty consultation. Even in these cases, however, reasonable care can be instituted based on a syndromic diagnosis. An "AMPLE" history may aid in establishing this diagnosis:

A allergies, arthropod exposures;
M medications, as well as military occupational specialty and mission-oriented protective posture status;
P past illnesses and vaccinations;
L last meal eaten; and
E environment/events preceding incident.

A brief but focused physical examination, even one performed by relatively inexperienced practitioners, can reveal at a minimum whether a victim of a biological or chemical attack exhibits primarily respiratory, neuromuscular, or dermatologic signs, or suffers from an undifferentiated febrile illness. By placing patients into one of these broad syndromic categories, empiric therapy can be initiated (see step 6). This empiric therapy can be refined and tailored once more information becomes available.[41,42]

When the situation permits, laboratory studies should be obtained to assist with later definitive diagnosis. Suggested laboratory studies, not all of which will be applicable in every case, are listed in Exhibit 20-2. On the battlefield, samples obtained at lower echelons are normally submitted to the local clinical laboratory and proceed through clinical laboratory channels to the 1st or 9th Area Medical Laboratory. Area medical laboratories, descendents of the 520th Theater Army Medical Laboratory, are theater-level tactical laboratories with robust scientific capabilities, including the ability to rapidly identify biological, chemical, and radiological threat agents, as well as endemic, occupational, and environmental health hazards. The area medical laboratories have reach-back ability and work closely with national laboratories at USAMRIID and the US Army Medical Research Institute of Chemical Defense.

Step 6: Provide Prompt Therapy

Once a diagnosis (whether definitive or syndromic) is established, prompt therapy must be provided. In the cases of anthrax and plague, in particular, survival is directly linked to the speed with which appropriate therapy is instituted. A delay of more than 24 hours in the treatment of either disease leads to a uniformly grim prognosis. When the identity of a bioterrorist agent is known, the provision of proper therapy is straightforward.

EXHIBIT 20-2

SAMPLES TO CONSIDER OBTAINING FROM POTENTIAL BIOWARFARE/BIOTERRORISM VICTIMS*

- Complete blood count.
- Arterial blood gas.
- Nasal swabs for culture and PCR.
- Blood for bacterial culture and PCR.
- Serum for serologic studies.
- Sputum for bacterial culture.
- Blood and urine for toxin assay.
- Throat swab for viral culture, PCR, and ELISA.
- Environmental samples.

*This list is not all-inclusive, nor is it meant to imply that every sample should be obtained from every patient. In general, laboratory sampling should be guided by clinical judgment and the specifics of the situation. This is a list of samples to consider obtaining in situations in which the nature of an incident is unclear and empiric therapy must be started before definitive diagnosis.
ELISA: enzyme-linked immunosorbent assay
PCR: polymerase chain reaction

TABLE 20-2

RECOMMENDED THERAPY FOR (AND PROPHYLAXIS AGAINST) DISEASES CAUSED BY CATEGORY A BIOTHREAT AGENTS

Condition	Adults	Children
Anthrax, inhalational, therapy* (patients who are clinically stable after 14 days can be switched to a single oral agent [ciprofloxacin or doxycycline] to complete a 60-day course†)	Ciprofloxacin‡ 400 mg IV q12h OR Doxycycline 100 mg IV q12h AND one or two additional antimicrobials§	Ciprofloxacin‡ 10–15 mg/kg IV q12h OR Doxycycline 2.2 mg/kg IV q12h AND one or two additional antimicrobials§
Anthrax, inhalational, postexposure prophylaxis (60-day course†)	Ciprofloxacin 500 mg PO q12h OR Doxycycline 100 mg PO q12h	Ciprofloxacin 10–15 mg/kg PO q12h OR Doxycycline 2.2 mg/kg PO q12h
Anthrax, cutaneous in setting of terrorism, therapy¶	Ciprofloxacin 500 mg PO q12h OR Doxycycline 100 mg PO q12h	Ciprofloxacin 10–15 mg/kg PO q12h OR Doxycycline 2.2 mg/kg PO q12h
Plague, therapy	Streptomycin 1 g IM twice daily OR Gentamicin 5 mg/kg IV or IM qd OR Doxycycline 100 mg IV or PO q12h OR Ciprofloxacin 400 mg IV or PO q12h	Streptomycin 15 mg/kg IM twice daily OR Gentamicin 2.5 mg/kg IV or IM q8h OR Doxycycline 2.2 mg/kg IV or PO q12h OR Ciprofloxacin 15 mg/kg IV or PO q12h
Plague, prophylaxis	Doxycycline 100 mg PO q12h OR Ciprofloxacin 500 mg PO q12h	Doxycycline 2.2 mg/kg PO q12h OR Ciprofloxacin 20 mg/kg PO q12h
Tularemia, therapy, and prophylaxis	Same as for plague	Same as for plague
Smallpox, therapy	Supportive care	Supportive care
Smallpox, prophylaxis	Vaccination may be effective if given within the first several days after exposure	Vaccination may be effective if given within the first several days after exposure
Botulism, therapy	Supportive care; antitoxin may halt the progression of symptoms but is unlikely to reverse them	Supportive care; antitoxin may halt the progression of symptoms, but is unlikely to reverse them
Viral hemorrhagic fevers, therapy	Supportive care; ribavirin may be beneficial in select cases	Supportive care; ribavirin may be beneficial in select cases

*In a mass casualty setting, where resources are severely constrained, oral therapy may need to be substituted for the preferred parenteral option.
†If the strain is susceptible, children may be switched to oral amoxacillin (80 mg/kg/day q8h) to complete a 60-day course. It is recommended that the first 14 days of therapy or postexposure prophylaxis, however, include ciprofloxacin and/or doxycycline, regardless of age. A three-dose series of Anthrax Vaccine Adsorbed may permit shortening of the antibiotic course to 30 days.
‡Levofloxacin or ofloxacin may be acceptable alternatives to ciprofloxacin.
§Other antimicrobials with in-vitro activity include rifampin, vancomycin, chloramphenicol, imipenem, clindamycin, or clarithromycin. Doxycycline is not recommended for treating cases with meningoencephalitis due to poor central nervous system penetration.
¶Ten days of therapy may be adequate for endemic cutaneous disease. A full 60-day course is recommended in the setting of terrorism, however, because of the possibility of a concomitant inhalational exposure.

(Table 20-2 *continues)*

Table 20-2 *continued*

h: hours; IM: intramuscular; IV: intravenous; q: each, every; qd: every day; PO: by mouth
Data sources: (1) Centers for Disease Control and Prevention. Update: investigation of bioterrorism-related anthrax and interim guidelines for exposure management and antimicrobial therapy, October 26, 2001. *MMWR Morb Mortal Wkly Rep*. 2001;50:909–919. (2) Centers for Disease Control and Prevention. Update: investigation of anthrax associated with intentional exposure and interim public health guidelines, October 19, 2001. *MMWR Morb Mortal Wkly Rep*. 2001;50:889–893. (3) Centers for Disease Control and Prevention. Notice to readers: additional options for preventive treatment for persons exposed to inhalational anthrax, December 21, 2001. *MMWR Morb Mortal Wkly Rep*. 2001;1142. (4) Inglesby TV, Dennis DT, Henderson DA, et al. Plague as a biological weapon–medical and public health management. *JAMA*. 2000;283:228–2290. (5) Inglesby TV, Dennis DT, Henderson DA, et al. Tularemia as a biological weapon—medical and public health management. *JAMA*. 2001;285:2763–2773. (6) FM 8-284 Working Group. Field Manual 8-284, AFJMAN 44-156, NAVMED P-5042, MCRP 4-11.1C. Treatment of Biological Warfare Agent Casualties. Fort Sam Houston, TX: US Army Medical Department Center and School; 17 July 2000.

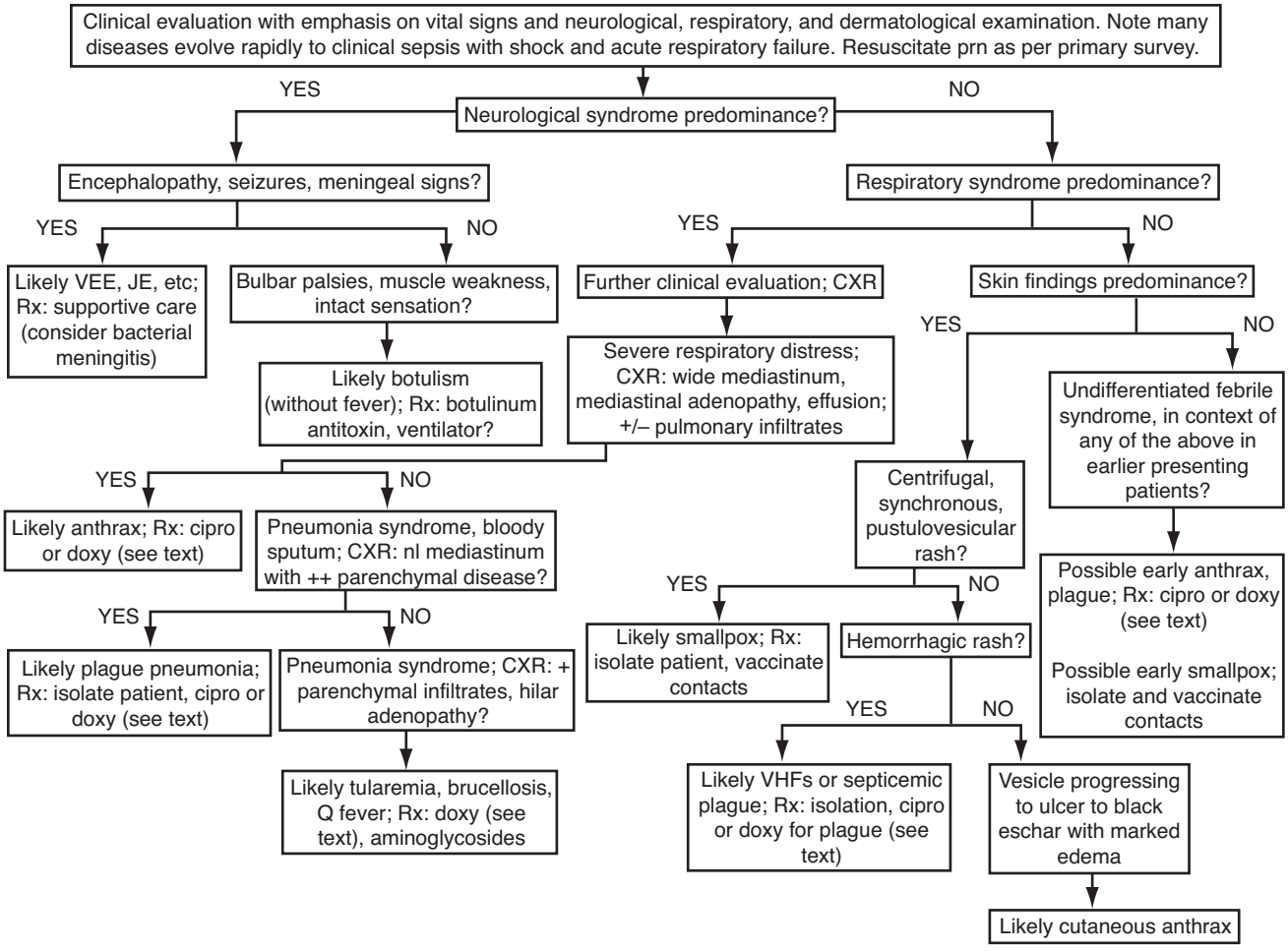

Fig. 20-2. An empiric and algorithmic approach to the diagnosis and management of potential biological casualties.
cipro: ciprofloxacin; CXR: chest X-ray; doxy: doxycycline; JE: Japanese encephalitis; nl: normal limits; prn: as needed; Rx: prescription; VEE: Venezuelan equine encephalitis; VHF: viral hemorrhagic fever; +: positive finding; ++: strongly positive finding; +/–: with or without finding.
Adapted with permission from Henretig FM, Cieslak TJ, Kortepeter MG, Fleisher GR. Medical management of the suspected victim of bioterrorism: an algorithmic approach to the undifferentiated patient. *Emerg Med Clin North Am*. 2002;20:351–364.

Recommendations for this therapy are provided in Table 20-2. When a clinician is faced with multiple patients and the nature of the illness is unknown, empiric therapy must be instituted. Guidelines for providing empiric therapy in these situations have been published,[7] and an algorithmic approach to syndromic diagnosis and empiric therapy is provided in Figure 20-2. Specifically, doxycycline or ciprofloxacin (Bayer AG, Leverkusen, North Rhine-Westphalia, Germany) should be administered empirically to patients with significant respiratory tract symptoms when exposure to a biological attack is considered a possibility.

Step 7: Institute Proper Infection Control Measures

The clinician must practice proper infection control procedures to ensure that contagious diseases are not propagated among patients. The majority of biological threat agents are not contagious, including the following causative agents:

- anthrax,
- tularemia,
- brucellosis,
- Q fever,
- alphaviral equine encephalitides,
- glanders,
- melioidosis, and
- many others (including all of the toxins).

When dealing with these diseases, standard precautions usually suffice.[43] More stringent, transmission-based precautions should be applied in certain circumstances. Three subcategories of transmission-based precautions exist:

1. Droplet precautions are required to manage persons with pneumonic plague. Ordinary surgical masks are a component of proper droplet precautions and constitute adequate protection against acquisition of plague bacilli by the aerosol route.

TABLE 20-3

CONVENTIONAL AND POTENTIAL INFECTIOUS DISEASES: REQUIRED HOSPITAL INFECTION CONTROL PRECAUTIONS*

Standard Precautions (handwashing)	Contact Precautions (gloves and gown†)	Droplet Precautions (private room‡, surgical mask§)	Airborne Precautions (private room‡, negative pressure room, HEPA filter mask)
Anthrax	VRE	Resistant pneumococci	Measles
Botulism	Enteric infections	Pertussis	Varicella
Tularemia	Skin infections	Group A streptococci	Smallpox¥
Brucellosis	Lice	Mycoplasma	Certain VHFs¥
Q fever	Scabies	Adenovirus	– Ebola
Glanders	*Clostridium difficile* disease	Influenza	– Marburg
Melioidosis	RSV	Pneumonic plague	– Lassa fever
Ricin intoxication	Certain VHFs¥	Meningococcal disease	Pulmonary TB
SEB intoxication	– Ebola		
T-2 intoxication	– Marburg		
VEE, EEE, WEE	– Lassa fever		
	MRSA		
	Smallpox¥		

*Thorough guidelines on hospital infection control can be found in Garner JS. Guidelines for isolation precautions in hospitals. The Hospital Infection Control Practices Advisory Committee. *Infect Control Hosp Epidemiol*. 1996;17:53–80.
†Gloves and/or gown should also be worn as a part of standard precautions (and other forms of precaution) when contact with blood, body fluids, and other contaminated substances is likely.
‡Mixing patients with the same disease is an acceptable alternative to a private room.
§Surgical masks should also be used as a part of standard and contact precautions (along with eye protection or a face shield) if procedures are likely to generate splashes or sprays of body fluids.
¥Indicated for both contact and airborne precautions.
EEE: eastern equine encephalomyelitis; HEPA: high-efficiency particulate air; MRSA: methicillin-resistant *Staphylococcus aureus*; RSV: respiratory syncytial virus; TB: tuberculosis; VEE: Venezuelan equine encephalitis; VHF: viral hemorrhagic fever; VRE: vanocomycin-resistant enterococci; WEE: western equine encephalomyelitis

2. Contact precautions should be used to manage certain viral hemorrhagic fever patients.
3. Airborne precautions, ideally including an N-95 HEPA filter mask, should be used to care for persons with smallpox.

A summary of hospital infection control precautions, as they apply to persons affected by biological terrorism, is presented in Table 20-3.

Step 8: Alert the Proper Authorities

As soon as it is suspected that a case of disease might be the result of exposure to biological or chemical agents, the proper authorities must be alerted so that appropriate warnings can be issued and outbreak control measures implemented. On the battlefield and in other military settings, the command must be notified immediately. It is similarly important, however, to notify preventive medicine officials and laboratory personnel, as well as the Chemical Corps. Early involvement of preventive medicine personnel ensures that an epidemiological investigation is begun promptly (see step 9) and that potential victims (beyond the index cases) are identified and treated early, when treatment is most beneficial. Notifying laboratory personnel not only permits them to focus their efforts on diagnosis, but also allows them to take the necessary precautions. Early notification of Chemical Corps personnel allows for battlefield surveillance, detection, and delineation of the limits of contamination. Using M93 "Fox" nuclear, biological, and chemical reconnaissance vehicles (General Dynamics Land Systems [Sterling Heights, Mich]/Thyssen-Henschel [currently integrated into Rheinmetall AG, Dusseldorf, Germany]; Figure 20-3), personnel can collect soil, water, and vegetation samples; mark areas of contamination; and transmit data to commanders in real time. As the transformation of the US Army progresses, the M93 "Fox" will be replaced by a "Stryker-Platform" NBC Reconnaissance Vehicle, which will also subsume the capabilities and functions of the BIDS system.[44]

Fig. 20-3. The M93 "Fox" nuclear, biological, and chemical reconnaissance vehicle.

In a civilian terrorism response scenario, notification of a suspected biological, chemical, or radiological attack would typically be made through local or regional health department channels. In the United States, a few larger cities have their own health departments. In most areas, however, the county represents the lowest governmental entity at which an independent health department exists. In some rural areas lacking county health departments, practitioners would access the state health department directly. Once alerted, local and regional health authorities are knowledgeable about mechanisms for requesting additional support from health officials at higher jurisdictions. Each practitioner should have a point of contact with such agencies and be familiar with mechanisms for contacting them before a crisis arises. A list of useful points of contact is provided in Exhibit 20-3.

If an outbreak proves to be the result of terrorism, or if the scope of the outbreak overwhelms local resources, a regional or national response becomes imperative. Under such circumstances, an extensive number of supporting assets and capabilities may be summoned. The National Incident Management System and its component Incident Command System provide a standardized approach to command and control at an incident scene.[45] Local officials use the Incident Command System when responding to natural and human-caused disasters, and the Incident Command System would be equally applicable in responding to a biological attack. Under the Incident Command System, a designated official, typically the fire chief or the chief of police, serves as local incident commander. The incident commander may have the ability to summon groups of volunteer medical personnel through the Metropolitan Medical Response System, which includes medical strike teams in 125 local jurisdictions. These teams, under contract with mayors of the 125 municipalities, are organized under the Department of Homeland Security's Office of Domestic Preparedness.

In any incident or disaster, whether natural or manmade, the local incident commander may request assistance from the state through the state coordinating officer, if it appears that local resources or capabilities will be exceeded. The state coordinating officer works with the governor and other state officials to make state-level assets (eg, state health departments, state public health laboratories, and state police assets) available. Most state public

health laboratories participate as reference (formerly level B/C) laboratories in the Laboratory Response Network, a collaborative effort of the Association of Public Health Laboratories and CDC. These facilities support hundreds of sentinel (formerly level A) laboratories in local hospitals throughout the nation, and they can provide sophisticated confirmatory diagnosis and typing of biological agents.[46,47] (An overview of public health laboratory capabilities is provided in Exhibit 20-4. The biosafety-level[48] precautions used by these laboratories are outlined in Exhibit 20-5.) State police can provide law enforcement assistance, and state police laboratories can assist with forensic analysis. Governors can access military assets at the state level through National Guard units under their direct control. These units can provide law enforcement, public works assistance, mobile field hospital bed capacity, and other support. Virtually every state governor now has one of 55 military Weapons of Mass Destruction-Civil Support teams. These 22-person advisory teams can offer expertise and provide liaison to additional military assets at the federal level.

When state capabilities are overwhelmed or insufficient, the state coordinating officer can alert the federal coordinating officer, who can, in turn, assist in activating the National Response Plan (see chapter 19 for related information). The National Response Plan guides delivery of federal assets and provides for a coordinated multiagency federal response. Federal response and support to state and local jurisdictions, according to the National Response Plan, are organized into 15 emergency support functions. Emergency

EXHIBIT 20-3

POINTS OF CONTACT AND TRAINING RESOURCES

Local law enforcement authorities*

Local or county health department*

State health department*

CDC emergency response hotline: 770-488-7100

CDC Bioterrorism Preparedness and Response Program: 404-639-0385

CDC emergency preparedness resources: http://www.bt.cdc.gov

Strategic National Stockpile: Access through state health department

FBI (general point of contact): 202-324-3000

FBI (suspicious package information): http://www.fbi.gov/pressrel/pressrel01/mail3.pdf

CBIRF: 301-744-2038

USAMRIID general information: http://www.usamriid.army.mil

USAMRICD training materials: http://ccc.apgea.army.mil

US Army medical NBC defense information: http://www.nbc-med.org

Johns Hopkins Center for Civilian Biodefense: http://www.hopkins-biodefense.org

University of Alabama, Birmingham, biodefense education: http://www.bioterrorism.uab.edu

Infectious Diseases Society of America: http://www.idsociety.org/bt/toc.htm

*Clinicians and response planners are encouraged to post this list in an accessible location. Specific local and state points of contact should be included.

CDC: Centers for Disease Control and Prevention; CBIRF: Chemical-Biological Incident Response Force; FBI: Federal Bureau of Investigation; NBC: nuclear, biological, and chemical; USAMRICD: US Army Medical Research Institute of Chemical Defense; USAMRIID: US Army Medical Research Institute of Infectious Diseases.

EXHIBIT 20-4

THE LABORATORY RESPONSE NETWORK

Sentinel Laboratories
These laboratories, found in many hospitals and local public health facilities, have the ability to rule out specific bioterrorism threat agents, to handle specimens safely, and to forward specimens to higher-echelon labs within the network.

Reference Laboratories
These laboratories (more than 100), typically found at state health departments and at military, veterinary, agricultural, and water-testing facilities, can rule on the presence of the various biological threat agents. They can use BSL-3 practices and can often conduct nucleic acid amplification and molecular typing studies.

National Laboratories
These laboratories, including those at CDC and USAMRIID, can use BSL-4 practices and serve as the final authority in the workup of bioterrorism specimens. They provide specialized reagents to lower level laboratories and have the ability to bank specimens, perform serotyping, and detect genetic recombinants and chimeras.

BSL: biosafety level
CDC: Centers for Disease Control and Prevention
USAMRIID: US Army Medical Research Institute of Infectious Diseases

support function 8 provides for health and medical services. Although a specific agency is assigned primary responsibility for each of the 15 emergency support functions, more than two dozen different federal agencies—as well as the American Red Cross—can, under federal law, provide assistance. Federal disaster medical support is primarily the responsibility of the Department of Health and Human Services, although the Office of Emergency Response—a component of the Department of Homeland Security—oversees the National Disaster Medical System.[49] A principal component of the National Disaster Medical System is its network of Disaster Medical Assistance Teams, each of which consists of trained medical volunteers with the ability to arrive at a disaster site within 8 to 16 hours. Another important component of the National Disaster Medical System is its excess hospital bed capacity, held at numerous Department of Veterans Affairs, military, and civilian hospitals throughout the nation.

Several other federal agencies may play an important role in the response to disasters, including, in particular, those resulting from a biological attack. The CDC and USAMRIID provide national (formerly level D) laboratories, which support the reference laboratories at the state level and are capable of handling virtually all potential biological threat agents.[50] Expert consultation and epidemiological investigative assistance are also available through the CDC, and bioweapons threat evaluation and medical consultation are available through USAMRIID. Additionally, the military can provide expert advice and assistance to civilian authorities through the Chemical/Biological Rapid Response Team, which can arrive at a disaster site within a few hours of notification, as well as through the previously described Chemical-Biological Incident Response Force, which is capable of providing reconnaissance, decontamination, and field treatment.[51] Similar to the Chemical/Biological Rapid Response Team, the Chemical-Biological Incident Response Force is trained and equipped to be available within hours of notification. Military support, when provided, is subordinate to civilian authorities. Military support would be provided and tailored by the Joint Task Force for Civil Support (Fort Monroe, Va), a component of US Northern Command (Peterson Air Force Base, Colo), which provides a command-and-control element for all

EXHIBIT 20-5

BIOSAFETY LEVELS

Biosafety Level 1
Involves practices used by a microbiology lab that deals only with well-characterized organisms that do not typically produce disease in humans. Work is conducted on open benchtops using standard microbiological practices. A high school biology lab might use BSL-1 practices.

Biosafety Level 2
Involves practices used by labs that deal with most human pathogens of moderate potential hazard. Lab coats and gloves are typically worn, access to the lab is restricted to trained personnel, and safety cabinets are often used. A clinical hospital laboratory would typically use BSL-2 practices.

Biosafety Level 3
Involves practices used by labs that work with agents with the potential to cause serious and lethal disease by the inhalational route of exposure. Work is generally conducted in safety cabinets, workers are often vaccinated against the agents in question, and respiratory protection is worn. Clothing (eg, scrub suits) is exchanged on exiting the lab. Labs are negatively pressurized. A state health department lab would typically use BSL-3 practices.

Biosafety Level 4
Involves practices used by labs working with highly hazardous human pathogens infectious via the inhalational route. BSL-4 organisms differ from those requiring BSL-3 precautions in that no vaccine or antibiotic therapy is available. Personnel may only enter and exit the lab through a series of changing and shower rooms. Equipment and supplies enter via a double-door autoclave. Strict and sophisticated engineering controls are used and personnel wear sealed positive pressure space suits with supplied air. Labs are negatively pressurized. Labs at CDC, USAMRIID, the Canadian Science Center for Human and Animal Health, and a few other research facilities are equipped with BSL-4 controls.

BSL: biosafety level
CDC: Centers for Disease Control and Prevention
USAMRIID: US Army Medical Research Institute of Infectious Diseases

military assets involved in disaster response missions and other contingencies within the United States. The CDC has developed the Strategic National Stockpile of critical drugs and vaccines necessary to combat a large disaster or terrorist attack, located at several locations throughout the country and available for rapid deployment to an affected area.[52] Release of stockpile components is currently controlled by the Department of Homeland Security.

Step 9: Conduct an Epidemiological Investigation and Manage the Psychological Aftermath of a Biological Attack

The clinician must understand the basic principles of epidemiology and be prepared to assist in the epidemiological investigation after a suspected terrorist attack. Although preventive medicine officers, environmental science officers, veterinarians, epidemiology technicians (91-S in US Army organizations), and field sanitation personnel may be invaluable during an investigation, the clinician should have a working knowledge of the steps involved in an epidemiological investigation. These steps, known as the epidemiological sequence, are published elsewhere[53] and summarized in Exhibit 20-6. Although the well-prepared clinician may have a positive impact on the health and well-being of individual patients, it is only through the rapid conduct of a competent epidemiological investigation that large numbers of exposed persons are likely to be reached, and successful medical and psychological prophylaxis implemented, before the widespread outbreak of disease or panic.

In addition to initiating an epidemiological investigation and specific medical countermeasures against biological agent exposures, the clinician should be prepared to address the psychological effects of known, suspected, or feared exposure to threat agents.[54] An announced or threatened biological attack can provoke fear, uncertainty, and anxiety in the population, and can result in an overwhelming number of patients seeking evaluation and demanding therapy for feared exposure. Such a scenario might also follow the covert release of an agent once the resulting epidemic is characterized as the consequence of a biological (or chemical or radiological) attack. Symptoms from anxiety and autonomic arousal, as well as side effects from postexposure to prophylactic drugs, may mimic prodromal disease from biological agent exposure and pose dilemmas in differential diagnosis. Persons with symptoms arising from naturally occurring infectious diseases may pose significant challenges to healthcare providers and public health officials.

Public panic and behavioral contagion are best prevented by timely, accurate, well-coordinated, and realistic risk communication from health and government authorities. Communication should include an assessment of the risk of exposure, information on the resulting disease, and a recommended course of action for suspected exposure. As the epidemic subsides and public knowledge increases, public anxiety will decrease to realistic and manageable levels. This cycle of uncertainty, panic, response, and resolution occurred during the October 2001 anthrax bioterror event.[55] Readily accessible (biological, chemical, and radiological), agent-specific information packages for local public health authorities and the general public are available through the CDC, and they can be of valuable assistance in risk communication.[56]

Effective risk communication is possible only in the presence of well-conceived risk communication plans and tactics that are worked out well in advance of an actual event. Similar advanced planning must consider the need to rapidly establish local centers for the initial evaluation and administration of postexposure prophylaxis. Development of patient and contact tracing mechanisms and vaccine screening tools, the mechanisms for accession of stockpiled vaccines and medications, and the means by which to identify and prepare local facilities and healthcare teams for the care of mass casualties must be clearly elucidated in advance. The CDC's Smallpox Response Plan[33] provides a useful template for a coordinated, multifaceted approach. The wisdom of farsighted planning and coordination was amply demonstrated by the efficient mass prophylaxis of more than 10,000 individuals in New York City during the events surrounding the discovery of anthrax-contaminated mail in 2001.[57]

EXHIBIT 20-6

THE EPIDEMIOLOGICAL SEQUENCE

1. Make an observation.
2. Count cases.
3. Relate cases to population.
4. Make comparisons.
5. Develop the hypothesis.
6. Test the hypothesis.
7. Make scientific inferences.
8. Conduct studies.
9. Intervene and evaluate.

Data source: Centers for Disease Control and Prevention. Investigating an outbreak. In: *Principles of Epidemiology: Self-Study Course 3030-G.* 2nd ed. Atlanta, Ga: CDC; 1998: 347–424.

Step 10: Maintain a Level of Proficiency

Once response plans have been developed, they must be exercised. Military commanders and their units are typically well versed in the planning and execution of conventional field training and command post exercises. In the future, however, these exercises must account for the real possibility that military units may encounter biological weapons on the battlefield. Similarly, planning and exercises must account for the tandem threat posed by bioterrorist attacks against garrison activities. Local civilian exercises (which can often include military participants) are a necessary component of disaster preparation. These exercises should be designed to test incident command and control, communications, logistics, laboratory coordination, and clinical capabilities. These exercises may involve only the leadership of an organization and focus on planning and decision making (the command post exercise), they may involve notional play around a tabletop exercise, or they may involve actual hands-on training and evaluation in a disaster drill or field-training exercise. The Joint Commission on the Accreditation of Healthcare Organizations requires hospitals to conduct a hazard vulnerability analysis, develop an emergency management plan, and evaluate this plan twice yearly; one of these evaluations must include a communitywide drill.[58] Moreover, the Joint Commission on the Accreditation of Healthcare Organizations specifically mandates that hospitals provide facilities (and training in the use of such facilities) for radioactive, biological, and chemical isolation and decontamination.

Many resources, including this textbook, are now available to assist both military and civilian clinicians and public health professionals in planning for, and maintaining proficiency in, the management of real or threatened terror attacks. Moreover, electronic resources of a similar nature have been developed[59,60] and multiple Web sites provide a wealth of training materials and information on-line [61] (see Exhibit 20-3) to assist military and civilian clinicians and public health professionals.

SUMMARY

To help manage the casualties that may result from biological warfare or terrorism, USAMRIID has developed a 10-step approach that specifies a tactical response as well as operational and strategic response. Military and civilian clinicians and public health professionals must be proficient in and plan for real or threatened terror attacks. Numerous governmental, military, and civilian organizations have now been organized, trained, and equipped to provide assistance and consultation to the clinician, first responder, and public health official faced with planning for, and treating, the victims of a potential terrorist attack. It is assistance that, if incorporated into thorough planning efforts, will hopefully never be needed for actual patient care purposes.

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