

Bioterrorism for the ER

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Course Objectives

Explore and define the role of the healthcare worker during a bioterrorism event.
Explain the roles of the various government agencies and managing a disaster.
Define the basic signs and symptoms of the five major weapons of mass destruction.

Introduction

The events of September 11, 2001, have increased concern about the potential use of biological, chemical, and nuclear weapons by terrorists. Medical and public health professionals will be the first respondents and they must be proficient in the recognition and management of these agents. The purpose of this course is to inform and educate attendees about biological, chemical, and nuclear events, specifically to (1) identify biological pathogens of concern for use in warfare or terrorism and the characteristics that make a biological pathogen an effective weapon; (2) describe the epidemiology, clinical features, medical management, and available treatment of potential medical problems derived from the use of biological, chemical, and nuclear weapons; and (3) understand the role of organized medicine in the national response to terrorism.

History and Overview of Weapons of Mass Destruction

Weapons of mass destruction (WMD) have been around since the 1700s, are easy to build, easy to hide, and pose a great threat. They are classified into three categories: chemical, nuclear, and biological weapons of mass destruction are attractive to potential terrorists because they create fear; are inexpensive; cause no damage to land or equipment; are difficult to detect; usually have no immediate clinical signs, ie: no burning on contact, invisible, and no taste or smell; and exhibit a delayed onset of symptoms -- nerve agents within minutes, vesicants within hours, and biological agents within days. With WMD, protection of large areas and large numbers of people is impossible. The disadvantages to WMD are contempt, retaliation, and prohibition treaties (all of which are now being ignored); danger during deployment due to accidents and no control over the wind; and the persistence of some agents.

Selected Facts About Anthrax

- Efficiency

30 kg anthrax spores = 30,000-100,000 deaths;

1,000 kg atomic bomb = 23,000-80,000 deaths.

Aircraft aerosol delivery of 100 kg anthrax spores on a clear, sunny day with a light

breeze would result in 130,000-460,000 deaths; on an overcast day or night with moderate wind 420,000-1,400,000 deaths; and on a clear, calm night 1-3 million deaths.

- Risks to healthcare workers include unsuspected agents, incomplete decontamination, inadequate ventilation, and the recent trend toward second bomb targeting responders.
- Diagnosis via gram stain, DFA, and culture.
- Cutaneous clinical - necrotic lesion that spontaneously heals (85%); Inhalation clinical -- 1- to 3-day incubation with fever, dyspnea, hemorrhagic mediastinitis and hypotension leading to death.

Selected Facts About Cyanide

- Inhibits cellular respiration by binding to the hemoglobin iron in the final step of the electron transport chain.
- Lethal plasma concentrations can be obtained quickly via the respiratory route.
- Cyanide is detoxified via rhodanese and b-Mercaptopyruvate-cyanide-sulfur transferase.
- Therapy: sodium nitrite bolus 300 mg dose given over 3 minutes to produce methemoglobin (usually >10%); sodium thiosulfate bolus dose (12.5 gm given over 10 minutes) to detoxify.
- In a mass causality situation the use of standard therapy would be difficult at best. Essential actions for WMD include prevention, preparation, detection, response, mitigation, treatment, prosecution, and reassessment. Prevention involves privacy, independence, and freedom issues; reducing government stockpiles; restricting availability of key equipment/supplies; and ensuring adherence to treaties/laws with stiff penalties for those found breaking the law. Preparation is required for medical supplies, protective equipment, detection technologies, personnel training, and command/control protocols. Detection includes the identification of agent(s), contaminated people, and contaminated equipment. Time, communication, and resource management are key elements of the response mechanism. Local personnel are the primary responders, with subsequent regional/state/federal support. Ultimate goals of a Terrorist Response Program are to save lives and, ideally, to obtain FDA approval of an antidote.

Expected toxicity of WMD is as follows:

- Organophosphate nerve agents -- rapid acting, acute and chronic CNS symptoms.
- Mustard gas -- delayed toxicity >24 hours; skin, eyes, and pulmonary
- Cyanide -- rapid acting
- Botulism -- 24-72 hours, needs extensive medical support, <10% fatality
- Anthrax -- 1-7 days, >95% fatality (inhalational).

Mitigation involves limiting contamination to existing casualties, preventing new casualties, achieving early decontamination (within minutes), isolating/protecting area of contamination, ventilating transportation and treatment areas, and watching for a "second bomb." Prompt treatment provides best outcome; successful treatment requires rapid identification of agents; late treatment requires supportive care and anticipation of sequelae of agents; and time and manpower demands will be intensive.

Prosecution requires collection of evidence from site and is often forgotten by healthcare providers. Reassessment includes learning from experience, identifying vulnerabilities/creating contingency plans, and including new personnel/obtaining their support.

The US policy on counterterrorism includes (1) the Presidential Decision Directive 39 (PDD-39) of 1995, which designates FBI as lead agency in crisis management response, FEMA as lead agency in consequence management response, and requires all federal agencies to support the Federal Response Plan; and (2) Defense Against Weapons of Mass Destruction Act (Nunn-Lugar-Domenici Bill) of 1996, which required the Secretary of Defense to establish a program to advise and train federal, state, and local officials until 1999 and allows the President or Attorney General to request military support for local authorities in chemical/biological incidents.

Bioterrorism: Threat Potential and Readiness Strategies

The US has dealt with WMD and biological warfare in the past but is now facing a composite continuum of issues concerning domestic biological terrorism. Terrorism acts since the early 1990s, including the Oklahoma City bombing (and a potential for more), have resulted in a new emphasis on WMD and a policy on counterterrorism. This type of event has been studied, anticipated, and practiced for five years; the new war is now a reality. A briefcase full of anthrax cannot be shot down. Medical personnel have a new role; the frontline force of protection and defense is medical in this new war. The vulnerability of the US lies in the fact that protecting large areas and large numbers of people is impossible. The US is a country of "haves" in a world of "havenots"; this has made the US a prime target, and the war will not be over in the foreseeable future.

Potential bioterrorism agents include *Bacillus anthracis*, *Yersinia pestis*, *Coxiella burnetii*, Ebola virus, *Vibrio cholerae*, and *Clostridium botulinum*. Recent events involving the weaponization of anthrax have resulted in 5 fatalities and 11 confirmed inhalational cases. It is estimated that *at least* 32,000 individuals have taken ciprofloxacin HCl (CIPRO, Bayer Corporation) in response to the threat posed by the distribution of anthrax spores through the US mail.

For several years, anthrax has been recognized as a potential biological threat to military as well as civilian populations. The causative organism of anthrax, *Bacillus anthracis*, occurs naturally, is relatively easy to access, is extremely resilient (in the spore form it may live for up to 50 years in soil), and is relatively inexpensive compared to conventional weapons. Anthrax spores range in size from 2 to 5 microns, just a fraction of the diameter of a human hair. Even a small number of anthrax spores, enough to fit on the head of a pin (approximately 5,000 to 8,000 spores), is sufficient to cause the inhalational form of anthrax. The inhalational form of anthrax is difficult to diagnose in the earliest stages, difficult or impossible to treat once clinical signs become apparent, and may allow only hours for therapeutic intervention. Its efficiency and low cost make anthrax accessible to virtually any group, including non-nation/state

terrorists. The anthrax organism that has been dispersed through the US mail appears to be a conventional strain of anthrax and is not known to be recombinant or genetically

altered. The protective antigen in anthrax binds with other proteins produced by the organism (edema factor and lethal factor). The resulting combination produces two highly virulent toxins, edema toxin and lethal toxin. This culminates in extensive, rapid-onset edema and hemorrhage. In the inhalational form of the disease, hemorrhagic lymphadenitis and hemorrhagic mediastinitis are manifest. Up to 50% of individuals with inhalational anthrax also develop hemorrhagic meningitis. The same process occurs with less severe consequences in cutaneous anthrax, emerging as an eschar on the skin associated with severe edema of surrounding tissue.

Anthrax vaccine was developed in the 1960s and is manufactured by BioPort Corp. in Lansing, Michigan. Because of FDA quality control issues, the entire amount produced has not been released. When the vaccine is administered, the antibody binds to receptor sites and precludes the ability of toxins to develop. The ability to understand the shape of these receptors will advance the development of antitoxins and possibly a better vaccine. In limited studies, more women than men have reported vaccine adverse reactions at the site of injection: 73% as opposed to 35%.

Current anthrax treatment recommendations have been outlined by the Centers for Disease Control and Prevention. Individuals with confirmed infections are generally treated with 2 or more antimicrobials administered intravenously. Treatment duration of 60 days is recommended unless follow-up testing rules out infection. High-dose penicillin (eg, amoxicillin or penicillin VK) when ciprofloxacin and doxycycline are contraindicated. Supplemental treatment recommendations include 7 to 10 days of corticosteroids for extensive edema involving the head/neck (cutaneous) as well as for pulmonary edema, respiratory compromise, and meningitis.

Smallpox is another potential bioterrorism agent. The US has only 15 million doses of the original vaccine. There is a current effort to dilute the vaccine 1:5 and assess its effectiveness in order to increase the number of people who can be vaccinated. Efforts to manufacture a new smallpox vaccine are currently under way. Smallpox vaccination in the US was discontinued 22 years ago; widespread immunization could resume within the next 2 years.

Bioterrorism is not always directed against people. Animal diseases can become a potential terrorist target. Foot and mouth disease has recently motivated eradication and control efforts in the UK, with more than 3.1 million animals killed; the US does not vaccinate cattle or swine against foot and mouth disease virus. There is no knowledge of how the disease was transported to the UK, but it was thought to have originated from the Pan Asian strain in China and could have been planted intentionally.

The bottom line is "What do we do about it and where do we go from here?" The US military has been concerned about bioterrorism outside its borders for years and has accumulated modular medical response data. In conventional warfare, local

emergency agencies use a "hot zone," "warm zone," and "cold zone" model. The hot zone comprises a bombed facility/area, and "first responders" -- emergency medical teams of firefighters, police, EMS, and ER personnel -- are at highest risk. With bioterrorism there is no definable hot zone or first responders. Among those at greatest risk of exposure to the agents of bioterrorism are those working in the medical community.

Emergency rooms throughout the US are working at 95% capacity. Currently there is little or no ability to effectively manage a sudden, simultaneous surge in patients. From 2005 to 2007 the number of US emergency rooms decreased more than 50% while ER visits increased 20%. Individual hospitals must be willing to address readiness issues in light of the new threats posed by bioterrorism.

The official tiered response consists of these four steps: Crisis/disaster event occurs; local responders become overwhelmed and state emergency management agencies arrive; the presence of additional personnel results in confusion and chaos; and federal emergency response teams arrive. Depending on the nature of the crisis, confusion and bureaucracy may actually interfere with an effective and timely response. The goal of an effective readiness strategy is to increase awareness of the gap between the time that local/state responders arrive/become overwhelmed and the time that federal assistance arrives. Current operational strategy with the Air Force Medical Service includes supporting Air Force bases with modular medical units using real-time epidemiology technology. This technology could be used effectively in US hospitals if civilian physicians are provided an opportunity to collaborate with Air Force medical personnel in the use of this specialized equipment. The Air National Guard medical service is particularly well positioned to rapidly augment civilian medical communities in crisis situations.

Unconventional warfare, terrorist attacks, anti-government protests, and other unclear threats are not likely to disappear. The key issue is how to prepare to respond. The US has the most capable medical system in the world and the most reliable response capabilities if they are used all together.

In post-Cold War America, concern that a biological "weapon" would *eventually* be deployed by a non-nation/state terrorist against civilian populations living in the US was highlighted by the recent injection of billions (estimate \$8.4 billion in the year 2000) of Federal dollars to establish a surveillance/ response infrastructure within the United States. At that time, most (although not all) authorities agreed that bioterrorism in the US was a very real and emerging threat for which the country was quite unprepared. That was before September 11, 2001, and before anthrax spores had been sent through the US mail, killing a few, exposing hundreds and scaring millions. Yet today, after continuing to pour billions more into defense against terrorism, the nation is still unprepared to meet the challenges of biological terrorism. Complacency, bureaucracy, organization, and economics are just some of the variables in a highly complex equation that underscore our vulnerability to catastrophic terrorism of the biological kind. By its very nature, *bioterrorism* is *medical* in nature and, as such, mandates

that we possess an organized, swift, and effective medical response capable of meeting the health care needs of perhaps thousands of simultaneous lethal and nonlethal casualties. But, do we really understand the nature of the biologic threat(s) facing us today? Is the medical community really prepared to manage a large-scale response and do so without becoming the "canaries in the coal mine"?

Every year the Department of State, in collaboration with the intelligence community, produces a report entitled *Patterns of Global Terrorism*. The latest report describes and analyzes terrorist events through the year 2005 and attempts to identify trends in terrorism. *Patterns of Global Terrorism 2005* is an unclassified and authoritative statement by the US Government on the recent history and evolving nature of terrorist threats to the United States. Representative James Saxon, Chair of the Special Oversight Panel on Terrorism, recently highlighted a few of these:

- During the year 2000, compared to 1999, international terrorists inflicted an increased number of casualties worldwide and increased the number of attacks against the United States specifically. Globally, the number of attacks by international terrorists rose from 392 in 1999 to 423 in the year 2000. Attacks against the United States increased from 169 in 1999 to 200 in the year 2000.
- During the year 2000, the single deadliest attack against the United States by international terrorists was the bombing of the USS Cole. This terrorist attack, on October 12 in the Yemeni port of Aden, killed 17 sailors and wounded dozens of others. The attack also incapacitated a sophisticated US guided missile ship, valued at a billion dollars that is vital to the security of our aircraft carrier groups and our presence in the Persian Gulf.
- Who are the nations that sponsor international terrorism? Some states might resort to terrorism as a form of asymmetrical warfare against the United States in a future crisis or conflict. Or they might use terrorism as part of a protracted campaign to attempt to force the United States to abandon its global role and its regional interests and allies.

Patterns of global terrorism 2000. identifies seven governments that sponsor terrorism: Iran, Iraq, Cuba, North Korea, and Sudan. The report also identifies Pakistan and Libya as governments of concern. Ironic as it may seem, at least two of these countries have earned status (post-September 11) as political allies in America's international fight against terrorism.

Patterns of global terrorism 2000 also notes that state-sponsored terrorism is being superseded by non-state sponsored terrorists. These non-state terrorists constitute a web of informally linked individuals and groups that have been involved in most of the major terrorist attacks or plots against the United States over the past 15 years. Nonstate terrorists now collaborate in terrorist acts throughout the world. Their destructive influence literally spans the globe, reaching from the Philippines to the Balkans, from Central Asia to the Persian Gulf, from Western China to Somalia, and from Western Europe to South Asia.

The Agents of Greatest Concern

As stated in the *MMWR*, April 21, 2000/49(RR04);1-14, "The public health infrastructure must be prepared to prevent illness and injury that would result from biological and chemical terrorism, especially a covert terrorist attack. As with emerging infectious diseases, early detection and control of biological and chemical attacks depends on a strong and flexible public health system at the local, state, and federal levels. In addition, primary health-care providers throughout the United States must be vigilant because they will probably be the first to observe and report unusual illness or injuries."

Where Do We Stand Today?

Recent Senate hearings on whether the United States was prepared to handle a "terrorist" attack on US soil found that a maze of 46 government agencies and multiple congressional committees have jurisdiction over the issue. This, in fact, may pose one of the most significant threats to any attempt to carry out an effective response effort . . .

Who's in charge?

On another note, a report recently published in the *American Journal of Public Health* (Wetter et al: *Am J Public Health* 2001; 91:710-717) suggests that few US hospitals are prepared to handle victims of chemical or biological terrorism such as the 1995 nerve gas attack in a Tokyo subway. Results from a survey of nearly 200 hospital emergency departments indicated that fewer than 20% had plans for dealing with patients exposed to biological or chemical weapons (eg, anthrax or sarin -- the nerve gas used in the 1995 Tokyo subway disaster).

Specifically, the study looked at whether the hospitals had sufficient antibiotics to treat 50 anthrax victims or even had the equipment to manage 50 sarin victims. Hospitals were also asked whether they had overall plans of action for biological and chemical terrorism. Urban hospitals were three times as likely to have such plans as rural hospitals were. More than 60% of the hospitals surveyed were in rural areas, and all hospitals were in four states: Alaska, Idaho, Oregon, and Washington. More than one third of all hospitals lacked sufficient antibiotic supplies to handle the anthrax scenario and just 29% had enough of the drug atropine to treat sarin patients. Far fewer had the decontamination facilities and other supplies for handling a sarin attack. Just 6% had all of the "minimum recommended physical resources" to deal with a sarin incident.

Response Plan Facts

- The threat of chemical and biological terrorist attacks against the United States is a national security concern. Strengthening response capabilities has been one reaction to the threat resulting in the establishment of federal stockpiles of antibiotics, antidotes, and other medical supplies. These stockpiles have been established and maintained by a number of different federal departments and agencies.
- Presidential Decision Directive 62 (PDD-62) designates the Department of Health and Human Services (HHS) as the lead federal agency to plan and prepare for a national response to medical emergencies in the event of a Weapons of Mass Destruction (WMD) attack. The Office of Emergency Preparedness (OEP) takes the

lead for these activities within HHS.

- The Federal Emergency Management Agency (FEMA) has the authority to release medical resources and other supplies in the event of a disaster or emergency declared by the President. FEMA coordinates the federal response through the federal response plan (FRP) which details the roles and responsibilities of federal agencies during national emergencies.
- Local governments have much of the initial burden and responsibility for providing effective medical response to a terrorist attack with support from state and federal agencies when appropriate. Local public health systems will be called upon to provide protective and responsive medical measures for affected populations, such as patient care, immunizations or prophylactic drug treatments for exposed groups, fatalities and decontamination of the environment.
- If a terrorist event overwhelms local and state authorities and requires a presidential disaster declaration, FEMA will implement the Federal Response Plan (FRP) and coordinate not only its own response activities, including the dispatching of federal pharmaceutical stockpiles, but also those of as many as 28 other federal agencies that may provide assistance.
- The release of biological or chemical agents will require rapid access to large quantities of pharmaceutical antidotes, antibiotics and/or vaccines. These pharmaceuticals may not be available in the amount or locations where they would be needed unless special stockpiles are created.
- The Department of Health and Human Services has addressed the need for pharmaceuticals and medical supplies through the Centers for Disease Control and Prevention's (CDC) National Pharmaceutical Stockpile (NPS) program and through the Office of Emergency Preparedness' National Pharmaceutical Stockpile.
- The Department of Defense (DOD) Chemical and Biological Incident Response Force (CBIRF) also maintains pharmaceutical stocks that can be used in a civilian emergency under certain circumstances.

Terrorism: Chemical and Biological Medical Supplies Are Poorly Managed, the GAO examined the management of pharmaceutical and medical supplies set aside for use in the event of a chemical or biological terrorist incident. The report found OEP, CDC, VA, and CBIRF lacked the internal controls needed to manage the supplies effectively. Poor management of the supplies resulted in overages, shortages, discrepancies in inventory records, expired items, and a lack of security measures. In order to address these problems, GAO listed four recommendations to strengthen internal controls, including (1) conducting risk assessments, (2) arranging for periodic, independent inventories of the stockpiles, (3) implementing a tracking system that retains complete documentation for all supplies ordered, received, and destroyed, and (4) rotating stock properly.

Conclusion

The threat of terrorism directed against civilian populations within the US has been validated. Although definitive proof that the use of "weaponized" anthrax is linked to international terrorist organizations is lacking, it could be argued that terrorism, especially involving pathogenic organisms, poses one of the most significant risks to

the public health of Americans today. It could also be argued that among the greatest of risks we face today is failing to prepare to respond. The ability of our nation to rapidly mobilize an effective medical response in the face of an incident of catastrophic terrorism is a deadly serious and complex issue that confronts the entire US medical community now.

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