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Dentistry and bioterrorism

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The dramatic events of September 11, 2001, and the harrowing days that followed are forever impressed on the minds of Americans. As the nation grieved for those lost in the attacks on the World Trade Center and the Pentagon, an assault was undertaken by as yet unknown individuals using the United States Postal Service to deliver mail contaminated with the deadly pathogen *Bacillus anthracis* [1,2]. Although the anthrax attacks had little direct impact on the economy or military preparedness of the nation, they dramatically revealed the world's potential vulnerability to the intentional release of biological agents as a terror weapon.

As a consequence of these events, national and local public health agencies, the military, civilian first-responders, and professional organizations have worked together to develop strategies to quickly identify, prevent, and mitigate any future biological attack. The role that dentistry will play in the event of a biological emergency, however, remains largely undefined. In June 2002, the American Dental Association (ADA) held a workshop on the role of dentistry in bioterrorism [3]. In March 2003, the United States Public Health Service and the ADA convened in a 2-day conference in Washington, DC, to better define the role of the dental profession in responding to bioterrorism or other catastrophic events [4].

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This article briefly summarizes the historical precedents for the use of biological weapons in war, describes the agents currently believed to pose the most likely threat for use as terror weapons, and discusses the role that dentistry might play in any future intentional use of biological agents.

History of biological warfare

Biological warfare, or *biowarfare*, has ancient roots. Long before recorded history, ancient man used biological toxins extracted from plants and animals on arrowheads or poison darts to kill game and human enemies. One of the earliest recorded uses of a biological weapon occurred in the sixth century BC, when the Assyrians poisoned enemy wells with rye ergot, a fungus that causes convulsions when ingested [5].

One of the most dramatic biowarfare events in history took place between 1345 and 1348. In 1345, a Mongol and Tartar army under command of Janibeg, Khan of the Golden Horde, besieged the Genoese-controlled city of Caffa in Crimea. The attack bogged down and the battle wore on into 1346. Complicating the military stalemate, plague soon arrived via the Silk Road from China, quickly engulfing the attacking army. In a desperate attempt to force an enemy surrender, the Mongol commander ordered his army to catapult plague-infected corpses over the walls of the city in a deliberate attempt to induce an epidemic of plague within the fortified enclave. Although the Genoese responded by dumping the corpses into the sea, plague quickly spread among the city's inhabitants. As the epidemic continued for the next 2 years, sailors fleeing Caffa by sea soon spread plague to ports throughout the Mediterranean, likely hastening the spread of the "Black Death" across Europe [6].

On this continent, General Jeffrey Amherst, Commander of the British forces during the French and Indian Wars, ordered the deliberate infection of Native Americans with smallpox by offering contaminated blankets to tribes that were allied with France. The ploy worked—most of the tribes were decimated by the subsequent infection, rendering them militarily ineffective [7]. This episode offers a sad footnote to the overall impact of smallpox on the indigenous inhabitants of the Americas. The unintentional introduction of smallpox into the valley of Mexico in 1520 by Spanish conquistadors may have killed as many as 8 million people and eventually led to the military defeat of the great Aztec confederation. Ultimately, smallpox and other Old World diseases resulted in the deaths of millions of immunologically naïve Native American peoples—leaving the North American continent largely open to European colonization [8].

During World War I, German agents posing as dockworkers used a mixture of glanders and anthrax that had been developed by Dr. Anton Dilger, an American-born, German-trained physician, to infect livestock destined for the Allies. Over 3000 cattle, horses, and mules were infected, as were several hundred military personnel [5].

During World War II, General Ishi, commanding the Japanese army's notorious Unit 731 in Manchuria, used prisoners of war and Chinese nationals as test subjects for biowarfare experiments. Some estimates indicate that up to as many as 3000 people were killed during tests with agents including anthrax, cholera, typhoid, and plague [5].

By 1943, the United States also was conducting research on bioweapons. The United States offensive biological weapons program continued during the Cold War in response to intelligence concerning Soviet bioweapons development efforts. Presaging modern concerns about bioterrorism against civilian targets, military researchers in 1966 used nonpathogenic marker organisms to demonstrate that bacterial agents released in a single New York subway station could infect the entire system [9]. Public concern about the risks and ethics of offensive bioweapons efforts eventually led President Nixon to issue an executive order in 1969 ending all offensive biological and toxin weapon research, redirecting the effort to concentrate on biowarfare defense [10].

In 1972, most of the world's bioweapon-producing countries signed the Biological and Toxin Weapons Convention (BTWC), the first treaty banning an entire class of weapons [11]. Unfortunately, some countries—including Iraq and the former Soviet Union—actually intensified their production after signing the BTWC. During the Cold War, the Soviets aggressively weaponized many agents, including smallpox and anthrax [12]. Meselson and colleagues [13] reported an investigation of a tragic incident that occurred in the Soviet city of Sverdlovsk in 1979. In that incident, a biological weapons plant accidentally released aerosolized anthrax spores that infected at least 96 individuals living downwind from the facility; 64 individuals are known to have died.

Anthrax was the agent of choice for the Japanese religious cult known as Aum Shinrikyo in an abortive attempt to use aerosolized anthrax in a terror attack in Kameido, Japan, in 1993. The attack failed because they selected a nonpathogenic laboratory strain instead of a more virulent form of the organism [14].

The current threat

Terrorists and the foreign governments that support them are suspected of seeking chemical, biological, radiological, nuclear, and high-yield explosive weapons. Because chemical and biological weapons are inexpensive and easy to make, they have been called the "poor man's nuclear weapons." Politically or religiously motivated terrorists may choose to use such weapons either on the conventional battlefield to offset the United States and allied superiority in conventional arms or against civilian targets.

A number of agents have been developed or have the potential for use as bioweapons. One of the concerns is that many of these agents initially present with symptoms that can be categorized as influenza-like illnesses [15]. Almost all of these agents initially present with varying combinations of fever, head and body aches, malaise, fatigue, anorexia, nausea, vomiting, coughing, or mild chest discomfort.

The Centers for Disease Control and Prevention (CDC) have categorized these agents into three categories. Category A agents are easily disseminated or transmitted person-to-person with a high death rate and potential for major public impact, public panic, and social disruption. These high-priority agents demand special attention from emergency planners and public health agencies. Category B agents are the second-highest priority and are described as moderately easy to disseminate, with moderate illness and death rates requiring enhanced diagnostics and surveillance. Category C agents are readily available, easily produced and disseminated, and have the potential to cause high rates of illness and sometimes death [16].

The CDC assessment of the domestic public health threat from potential biological weapons agents has identified six category A agents [16]. These include anthrax, smallpox, pneumonic plague, tularemia, botulism toxin, and viral hemorrhagic fevers such as those caused by Ebola or Marburg virus. Of these agents, anthrax and smallpox have received the greatest attention on the part of disaster response planners; for the purposes of this article, detailed discussions are confined to these two organisms.

Anthrax

The anthrax-contaminated mail attacks in 2001 involved *B anthracis* spores that were smaller than the pores in the paper envelopes, allowing them to easily escape during mail processing. In the end, five letters mailed from Trenton, New Jersey, reached their intended destinations in Florida, New York City, and Washington, DC. Among those unsuccessfully targeted were two United States senators and a news anchorman for a major television network. However, 22 other individuals did become infected with either inhalational or cutaneous anthrax. Of the 11 inhalational cases, 5 died. Most were not recognized early enough during the course of their illness to allow potentially live-saving intervention. All of the 7 confirmed and 4 suspected cutaneous anthrax cases survived [1,17,18].

B anthracis spores are hardy and can survive for many years in soil. The spores germinate when introduced into a nutrient-rich environment, such as human or animal tissue. The suite of symptoms known as anthrax result from the formation of three principal exotoxins that produce hemorrhage, edema, and tissue necrosis [5,18]. Depending on the route of transmission, the bacillus produces three distinct clinical presentations described as inhalational, cutaneous, and gastrointestinal anthrax [5,18].

Anthrax is not transmitted from person to person. The cutaneous variant is the most common form with an estimated 2000 cases worldwide reported annually. Cutaneous disease is usually the result of bacteria entering the skin through scratches, abrasions, or—rarely—insect bites. It most frequently occurs in individuals who are occupationally exposed during the handling of infected animal products (eg, wool, hides) and results in the pathognomonic, coal-colored lesion that gives both the organism and disease its name [17]. If left untreated, cutaneous anthrax can result in up to 20% mortality; if treated, the mortality drops to less than 1% [18].

Gastrointestinal anthrax is usually transmitted by bacteria ingested through undercooked and contaminated meat [18–20]. The mortality ranges from 25% to 60% and is fortunately not as common as the cutaneous form [20]. An oropharyngeal variant has been reported in the literature and is discussed later in this section.

Inhalational anthrax occurs when *B anthracis* spores are drawn into the lungs during respiration. It is the deadliest form of anthrax, with mortality reaching up to 95% or more if therapy is not initiated until after onset of clinical symptoms [18,20]. Naturally occurring inhalational anthrax is exceedingly rare in the Unites States. There were only 18 cases reported in the United States between 1900 and 1976 [17].

Anthrax is an ideal biological agent because it is odorless, colorless, and tasteless. Its production requires only minimal expertise, and the equipment used to produce vaccines can also be used to produce the agent. The spores may be delivered in a variety of ways, but the most highly lethal form is as an aerosol. Other methods of delivery include contaminated food and surface contact [5].

Once infected, symptoms can occur within 7 days of the infection, although patients may remain asymptomatic for up to 60 days. Influenza-like symptoms such as fever, nonproductive cough, chest discomfort, shortness of breath, fatigue, muscle aches, sore throat, difficulty swallowing, enlarged lymph nodes, headaches, nausea, vomiting, and diarrhea may be present to varying degrees [15,18,20,21]. Unlike patients with inhalational anthrax, adults with influenza or other viral respiratory illnesses do not usually present with shortness of breath. In contrast, patients suffering from inhalational anthrax typically do not present with a sore throat or rhinorrhea, as is often seen with influenza or other viral respiratory illnesses [15,21].

Sirisanthana and Brown [19] described the clinical characteristics of an oropharyngeal variant of gastrointestinal anthrax. Symptoms may include fever, toxemia, or inflammatory lesions in the oral cavity or oropharynx with enlargement of cervical lymph nodes. Lesions form and typically progress to ulceration (though they may self-limit at any stage), and a pseudomembrane eventually develops over the ulcer. There is a high case–fatality rate. An outbreak of oropharyngeal anthrax that was reported in 1982 in the Chiang Mai province of Thailand was associated with consumption of undercooked meat from infected livestock. Of 76 reported cases, 24 presented with oropharyngeal symptoms including fever, sore throat, dysphagia, and respiratory difficulty. Acute inflammation was present in the oral cavity or oropharynx with lesions up to 6 cm in size on the tonsils, posterior pharyngeal wall, and hard palate. Enlargement of the neck was equally dramatic with associated lymph node involvement and soft tissue edema. In severe cases, the lesions spread to involve the uvula and soft palate as well as the anterior and posterior pillars of the fauces. Typical lesions consisted of early local edema and congestion progressing to central necrosis and ulceration producing a whitish patch. Surprisingly, there were no cases of classic gastrointestinal anthrax seen in this outbreak.

Cutaneous and gastrointestinal anthrax respond readily to antibiotic therapy. Inhalational anthrax can also be treated with both antibiotics and vaccine if the diagnosis is made after exposure but before the appearance of symptoms. Current regimens call for Ciproflaxacin (400 mg intravenously or 500 mg orally), or Doxycycline (100 mg intravenously or orally) twice a day with two additional antimicrobials such as Rifampin, Vancomycin, and Clindamycin. Initially, intravenous administration is recommended, switching to oral therapy when appropriate for a combined total 60 days of therapy. Because of poor compliance with prophylaxis regimens and the high level of exposure to anthrax spores in the postal system cases in 2001, two additional options for treatment have been recommended. These patients may take an additional 40 days of antibiotic therapy or three doses of anthrax vaccine over 4 weeks, plus an additional 40 days of antibiotics. Postexposure antibiotic therapy before the development of symptoms may be augmented with vaccine if the patient has not previously been vaccinated [18,20]. Adherence to vaccine regimens among individuals potentially exposed to anthrax spores in 2001 was poor, ranging from 21% to 64% [22].

An anthrax vaccine approved by the United States Food and Drug Administration is currently available. The vaccine must be administered in six doses over an 18-month period [18]. Because of concerns about possible military use of weaponized anthrax by potential adversaries, United States military personnel are currently receiving the vaccine as dictated by operational requirements.

Smallpox

The other major biological threat today is smallpox. The last outbreak of smallpox in the United States occurred in the Rio Grande Valley, Texas, in 1949 [8]. Two years earlier, an unrecognized hemorrhagic case from Mexico made its way to New York City. Prompt response by public health officials quickly brought the outbreak to a halt as over 6 million New York City residents received vaccinations [8]. In 1980, the World Health Organization declared the eradication of this ancient plague 3 years after the last naturally occurring infection was seen in Somalia. The United States public vaccination program ceased in 1972, with military vaccinations continuing until 1989 [8].

Smallpox is caused by the variola virus, which is found only in humans. There is no animal or environmental reservoir, and the only known stockpiles in the world are in the United States and Russia [5]. There is no specific treatment for the disease other than prevention. Expected mortality for clinical cases is approximately 30% [5].

The disease begins with an asymptomatic 7- to 17-day incubation period during which the patient is not contagious. Unfortunately, during this period patients may travel widely, potentiating the rapid spread of the disease. A prodromal period follows that lasts 2 to 4 days with characteristic influenza-like symptoms; at this time, the patient may become infective. At the conclusion of the prodrome stage, small red spots begin to develop on the tongue and mouth, transforming into sores that spread large amounts of virus into the mouth and throat. It is at this time that the patient is most contagious. An early rash develops on the face and spreads to the arms, legs, hands, and feet. The rash gives way to raised, fluid-filled bumps. A pustular rash soon develops, giving way to scabs and eventually resolution. The patient remains contagious until the scabs have completely resolved [5].

Smallpox is highly contagious and may be spread by aerosols, direct contact with infected bodily fluids, or contaminated objects (eg, bedding, clothing). Some estimates report that each contaminated individual could potentially spread the disease to 10 to 20 others. Strict isolation procedures including contact, droplet, and contact precautions are required to control the spread of smallpox in the hospital [5]. Smallpox virus in infected persons is usually shed from the epithelium of the naso-oropharynx and salivary glands. A recent editorial in the *Journal of Dental Research* urged the dental research community to place a high priority on studies of oropharyngeal shedding of poxviruses and potential means to interrupt disease transmission by this route [23].

The effect of weaponizing smallpox is difficult to quantify, but analyses of recent large-scale exercises are quite sobering. A tabletop exercise conducted in June 2001 and entitled "Dark Winter" simulated a smallpox outbreak beginning in Oklahoma City. With the intent of increasing awareness of the threat posed by biological weapons, experienced former officials played the roles of key officials from local, state, and federal governments. Despite simulated mobilization of local, state, and federal resources, the disease quickly spread to 25 states and 15 countries. Among other things, analysts concluded that an attack on the United States with biological weapons could threaten vital national security interests and that current organizational structures and capabilities are not well suited for the management of a biological attack [24].

Vaccination remains the most reliable means of preventing the spread of smallpox. For an unvaccinated population, epidemiological surveillance, rapid identification of index cases, quarantine, and mass vaccination are tools available to stem the spread of this disease throughout the population [25]. The smallpox vaccine is a live vaccine produced from the closely related vaccinia virus. Vaccination results in high-level immunity offering protection for 3 to 5 years in 95% of cases. It also appears to reduce the severity of disease for vaccinated persons for at least an additional 10 years. Revaccination may provide residual immunity for up to 30 years. Vaccination up to 3 days after exposure can prevent infection, while vaccination up to 7 days postexposure may substantially lessen severity of the disease [26].

Historically, smallpox vaccine has an excellent safety record; approximately 14 to 52 life-threatening reactions and 1 to 2 deaths per 1 million vaccinations were reported in a national survey conducted in 1968 [27]. Nevertheless, since universal vaccination programs ended over 30 years ago, the number of immunocompromised persons in the general population has increased, potentially increasing the pool of individuals at risk of complications associated with the use of live vaccines.

Contraindications to vaccination include pregnancy, immunosuppression, and skin conditions such as eczema [27]. The vaccine is not currently recommended for persons under the age of 18 [27]. Evidence from recently completed vaccinations of over 450,000 Untied States military and Department of Defense personnel revealed an incidence of adverse events below historical rates [28]. A study of United States military personnel receiving smallpox vaccination between December 2002 and March 2003, however, reported 18 cases of nonfatal myopericarditis among 230,734 primary vaccinees. No cases were reported among 95,622 previously vaccinated individuals. The incidence of myopericarditis among the primary vaccinees was 3.6 times greater than the natural background occurrence of this condition. The authors recommend that clinicians consider myopericarditis in the differential diagnosis of patients presenting with chest pain 4 to 30 days following smallpox vaccination.

Preparation and response to biological attacks

Among the factors complicating efforts to respond successfully to a large-scale biological attack is the lack of sufficient surge capacity to deal with the numbers of patients that will require prophylaxis or treatment. Nationwide shortages of health care workers, including physicians [29,30] and nurses [31], further contribute to official worries. Worldwide combat operations in the war on global terrorism and commitments to peacekeeping may also severely tax the capability of the United States military to respond to a domestic biowarfare attack. A mass casualty event, particularly one involving chemical or biological agents, has the potential to overwhelm the local medical system. Physicians, nurses, and other first responders may not be able to respond to the demand for services that will include the need to provide not only treatment and prophylaxis, but also reassurance. Other health professionals, including dentists, may need to step forward and fill this gap. To be effective, the dental profession must more clearly define its role in responding to biological emergencies.

A role for dentistry?

Recognizing the need to define the role of dentistry in a bioterrorist attack, the ADA convened in a workshop in June 2001 that was attended by leading bioterrorism experts [3]. It was one of the first attempts to develop a consensus on dentistry's role in these circumstances. In March 2003, the ADA and the United States Public Health Service jointly sponsored a conference entitled "Dentistry's Role in Responding to Bioterrorism and Other Catastrophic Events" [4]. Over 300 private practice and public health dentists, dental educators, military dental officers, dental researchers, and team members, including hygienists and assistants, were briefed by top officials, including the United States Surgeon General, on potential new roles for dentistry to supplement its traditional forensic mission in mass disaster management.

Conference attendees were advised that dental resources would likely be needed should conventional medical capabilities become overwhelmed following a major bioterrorism event. The ADA president and executive director announced the development of a strategy to educate dentists about their possible role following a biological attack.

Organized dentistry and dental educators must make a concerted effort to develop training programs that capitalize on the medical and scientific knowledge and clinical patient care skills of dentists. Programs designed to educate general dentists in emergency preparedness and emphasize the development of trainers to educate other health care professionals in emergency response and public health awareness are already underway.

Dentists can play an important role in protecting themselves, their patients, and the community by serving as a reliable and scientifically accurate source of information before, during, and after a biological emergency. Because of their knowledge of basic medicine and specialized expertise in diseases of the oropharynx, dentists may also serve as sentinels for early identification of a disease outbreak, whether it be naturally occurring or due to the action of individuals with inimical intent. Recently, the ADA collaborated with the CDC to distribute informative packages on the diagnosis and management of smallpox infections.

Supporting the ADA and the public health agencies, other professional associations, including the Academy of General Dentistry (AGD) and the Organization for Safety and Asepsis Procedures (OSAP), have featured continuing education on bioterrorism and have developed training programs to help dentists respond to such events. The AGD has encouraged the creation of disaster response courses for its state and local constituencies and has sponsored courses on disaster response at regional and national meetings in 2003 and 2004. OSAP has featured programs on bioterrorism, beginning with its Annual Symposium program in 2000, and provides updated information for dentists at its website. Extension of this concept into dental school curriculums should be encouraged.

The New York University (NYU) College of Dentistry has developed a program that will identify and train individuals in a defined curriculum of emergency response linked with public health awareness [32]. These trainers will then conduct training for other health professionals in surveillance of and response to emerging threats and catastrophic events. A goal of the NYU program will be the development of a qualifying certificate in emergency response and management.

During the 2001 anthrax attack, well-informed medical providers, including dentists, might have quelled some of the misinformation circulating among the public. During a bioterrorism event, an already overburdened health care system can be stretched even further as it seeks to cope with large numbers of the inevitable "worried well." By educating dentists in disease recognition, risk communication, patient education, triage, planning, and administration, it may be possible to extend the capacity and responsiveness of local health care systems. As respected health care professionals, well-informed dentists may be able to do much to help allay fear among members of the community.

Local dental societies and interested individuals must extend the offer to integrate community dental assets into local emergency response plans, bringing not only the capabilities of the dentist but also the skills of well-trained ancillary personnel. The decentralized pattern of distribution of dental offices in most cities makes them excellent locations for community-based distribution or immunization centers—potentially taking some of the burden away from hospitals and medical centers.

Dental offices also can serve as sentinels for community-wide epidemiological surveillance. With proper training, dentists can recognize characteristic intraoral and cutaneous lesions and alert the proper authorities of a suspected case involving bioterrorism. Recognition and reporting of abnormal patterns of employee absences and broken patient appointments could also signal the emergence of an infectious disease in a community.

After recognition of an outbreak and identification of the agent, dentists may be able to identify potentially infected individuals and refer them to a physician for confirmation. Dentists with proper training in administration of vaccines or antibiotics may also assist an overextended health care system by assisting in prophylaxis efforts. Within limitations imposed by dental practice acts, dentists could conceivably help free up physicians by serving as triage officers. In the military, dental officers have been very effective in this role during mass casualty situations, allowing physicians to treat casualties.

In the aftermath of catastrophic events, dentists may provide some of the treatment normally reserved for physicians and associated personnel. The degree of involvement will depend on the magnitude of the event and the individual skills and training of dentists. Some dentists with hospital training may help augment overextended medical staff. In a biological event, dental team members understanding of infection control principles can aid in preventing further spread of disease. With training, dental personnel can also support decontamination efforts.

Full integration of dentists in disaster response programs may require that they provide care outside of the traditional limits set by state dental practice acts. There are also concerns about potential liability for dentists operating outside of the normal scope of care. With proper training, however, dentists are capable of casualty triage; care of the injured; vaccinating and immunizing for life-threatening, terrorist-caused disease; and prescribing or dispensing for those conditions. Dental academia, organized dentistry, state licensing boards, and federal and state legislators must discuss the issues of training, certification, scope of care, and liability protection for properly trained responding dentists.

Summary

Dentistry's role in responding to bioterrorism and other catastrophic events is evolving and may involve a wide range of activities. Organized dentistry, local dental societies, and interested individuals should make local emergency response planners aware of the services the dental profession can provide and should work to integrate dental resources to strengthen the disaster response capacity of community health care systems. With effective planning, education, and training, dentists can play a significant role in responding to acts of bioterrorism or other unforeseen events.

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