COMMENTARY

A silent bomb: The risk of anthrax as a weapon of mass destruction

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No rational person can deny the destructive potential of a nuclear bomb as a weapon of mass destruction (WMD). The perception of anthrax as a WMD, however, is yet unformed in our society and its institutions. Opinions on anthrax WMD have ranged from dire to dismissive (1, 2), but a scientifically rigorous analysis of their destructive potential has been lacking. In a recent issue of PNAS, Wein, Craft, and Kaplan (3) filled this critical gap by providing quantitative assessment of the deaths resultant to a civilian population from an airborne attack of weaponized anthrax on a large city. The analysis in ref. 3 is a mathematical model, and, as such, is founded on scientific assumptions and framed in mathematical language. It is not a typical model of a scientific phenomenon, because of the irreducible uncertainty of its formulation and parameters. Its predictive power is thus subject to scientific debate. Nonetheless, this comprehensive model is the best information available to organize our understanding of anthrax as a WMD.

Public misconceptions exist in the areas of treatment, prevention, detection, and destructiveness with regard to the character of anthrax. First of all, it is not the bacteria, *Bacillus anthracis*, that poses the greatest risk, but its dry concentrated spores. Inhaled spores, several microns in diameter, reach deep into the lungs, then travel to lymph nodes, replicate in the blood, and produce toxins that cause mortal illness (4). Medical intervention may be successful, but timing is critical. Postexposure oral antibiotic prophylaxis is efficacious if begun during the presymptomatic incubation stage. Combination antibiotics and aggressive hospital supportive care may also succeed in the prodromal stage, but the disease is beyond treatment and inevitably fatal once the fulminant stage is reached (5). Vaccination is believed effective, although complete immunity requires a series of six shots over 18 months, followed by annual booster shots (6).

The detection of anthrax spores is difficult, and rapid in-place detection in the atmosphere is not yet technologically practical. The new Bio-Watch surveillance network announced by the U.S. Government on January 22, 2003, established monitoring systems to detect airborne anthrax, but the time lag is 12–24 h after release, and false positives or negatives are problematic (7, 8). The method of anthrax attack does not require intercontinental ballistic missiles or sophisticated aerial delivery systems. As President George W. Bush said in an address in Cincinnati on October 7, 2002, "all that might be required are a small container and one terrorist or Iraqi intelligence operative to deliver it" (9). By far the most serious failing in public comprehension of anthrax is the perception of its destructiveness. The quantification in ref. 3 leads us to a realization that the destructive capability of weaponized anthrax is equivalent to that of a nuclear bomb.

The main objective is to compare different strategies for treating symptomatics and asymptomatics.

The model in ref. 3 assumes a point-release of 1 kg of spores, concentrated at a trillion spores per gram, from a height of 100 m, in a city of 10 million inhabitants. The model is detailed in its consideration of the elements of the event: the geographical dispersion of the aerosolized spores, the exposure to and age-dependent dose–response of inhabitants, the dynamics of anthrax disease progression, and the timing and organization of medical intervention. These elements are specified in a system of 15 integro-partial differential equations with 36 parameters, which are elaborate but mathematically tractable (3).

The main objective in ref. 3 is to compare different strategies for implementing antibiotics and hospital care to symptomatics and asymptomatics. The strategies are based on a threshold parameter p that determines the fraction of all inhabitants that receive antibiotics in a time-varying geographical ring that grows as the fraction of inhabitants displaying symptoms exceeds p. Within the ring, people with symptoms immediately enter the local queues for antibiotics. If $p = 0$, both symptomatics and asymptomatics receive prophylactic antibiotics. If $p = 1$, only symptomatics do. The model incorporates availability and dispensation of hospital care to symptomatics by local or mobile (nonlocal) providers in several prioritization scenarios.

The model in ref. 3 provides a virtual construct for the reality of an actual attack. The conclusions drawn from computer simulations of the model are stunning, even in the base case ($p = 0$), when the postattack response is relatively efficient. In the base case, >100,000 deaths result in the population of 10 million inhabitants. Less aggressive distribution of antibiotics to asymptomatics ($p > 0$) increases this number up to 7-fold. Enhanced distribution capacity and supportive hospital care can significantly reduce deaths, and preattack distribution of antibiotics can reduce deaths by 50%. The number of deaths is not markedly reduced by rapid detection, however, even well below the base case value of detection at 48 h after release. If the detection delay is reduced to 6 h after release, ≈70,000 deaths are still incurred in the base case. If the detection delay is increased to 4.8 days after release, then the number of deaths in the base case is doubled. Further tuning of the model parameters adjusts the toll in lives by thousands, tens of thousands, or more.

Wein, Craft, and Kaplan discuss policy implications stemming from their model, and this is their most important contribution. The measures they recommend require economic costs and societal changes. If we rely solely on postattack logistical response, then we must better prepare public, medical, and government sectors. The key issues in postattack response are the efficient distribution of antibiotics to everyone in an afflicted region (both symptomatics and asymptomatics) and the efficient organization of acute hospital care for symptomatics. The U.S. Government has established emergency supplies of antibiotics and medical equipment in the National Pharmaceutical Stockpile (NPS; ref. 10). The NPS has sufficient ciprofloxacin to

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treat 12 million people for 60 days. So-called 12-h push packs from the NPS are in place to rush supplies to target locations within 12–24 h. The 12-h push packs include several hundred ventilators, which are, as noted in ref. 3, crucial for acute hospital care of inhalation anthrax disease. Most U.S. communities have only enough antibiotics, ventilators, and other essential hospital support equipment to meet routine on-going need, and thus, their dependence on NPS supplies is critical. In the event of a large-scale attack or multiple attacks, however, the NPS supply of antibiotics and other essential medical supplies, as well as the organization of local infrastructures for their allocation, are inadequate for the immense need.

Postattack response is essentially damage control. It is vital, but preattack measures are even more important. Wein, Craft, and Kaplan recommend preattack training of health care workers and preattack vaccination of all first-responders to sustain a postattack response. They also raise the possibility of preattack distribution of antibiotics, to be taken only if an attack occurs. There are serious issues to be addressed in this recommendation, including costs, administration, improper use, onerous side effects, antibiotic resistance, and the lack of medical supervision and control. Yet, the advantages may be crucial, and far outweigh the disadvantages. Most importantly, Wein, Craft, and Kaplan raise the possibility of preattack mass vaccination, which may be the most rational defense of our citizenry. Preattack vaccination of the entire U.S. population could be accomplished in a phased implementation within several years. The resulting reduction of risk of anthrax WMD could be far greater than the reduction of risk of nuclear WMD achieved by anti-ballistic missile systems.

There are forms of anthrax attack other than the large-scale release assumed in ref. 3. Small amounts of powdered anthrax inserted into the air intakes of subways, airports, shopping malls, sports arenas, and other public complexes could be devastating to the fabric of our open society. In the attacks on the U.S. postal system in the fall of 2001, six letters, each containing 1 or

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2 g of anthrax spores, caused five deaths (11). This anthrax was of a concentration and lethality comparable to that assumed in the model in ref. 3, and its origin is still unresolved (12). Wein, Craft, and Kaplan calculate the human costs of anthrax attacks, but economic costs should be counted as well. The decontamination of the Hart Senate Office Building in Washington, DC, required several months and ≈23 million dollars (13). The decontamination of the postal plants in Brentwood, DC, and Hamilton Township, NJ, required >1 year and >100 million dollars (14). The amount of anthrax involved in the contamination of each of these facilities was probably <1 g. The limiting factor in all calculations of the potential destruction of anthrax WMD, both human and economic, is the quantity of weaponized anthrax possessed by an enemy with the willingness and the capability to use it.

Public education underlies all biodefense policy. In the 1950s, school children were drilled in emergency civil defense exercises to be used in a case of nuclear attack. The value of these and other measures can be debated, but no one can doubt the value of biodefense education. An informed and prepared public will be far better equipped to withstand a crisis that, as Wein, Craft, and Kaplan write, "could degenerate into panic, flight, communications breakdown, economic disruption, and general societal dysfunction." As Jeanne Guillemin writes: "The power of terrorism lies in its threat of potential harm. To this coercion, the threat of biological weapons adds its own powerful symbolic implications of dissolution and despair. On a collective level, a major epidemic can destroy social order" (15).

Weaponized anthrax is, and will remain, a serious threat in the hands of psychopaths, terrorists, and malevolent regimes (16–18). But, unlike nuclear WMD, anthrax WMD are defensible. The challenge to science is to develop anthrax vaccines or antidotes that can be made available to every human being. In the meantime, the recommendations in ref. 3 are urgently required. In *The Guns of August* (19), Barbara Tuchman describes the ignorance and denial in European nations, at the advent of World War I, of the terrible destructiveness of modern warfare. In 1914, few foresaw that millions of soldiers and civilians would lose their lives in a war that would supposedly last only a few weeks. Are we at a moment in history when there is a lack of perception of the potential destructiveness of a new and unknown form of warfare? The mathematical model in ref. 3 quantifies the number of deaths we may sustain in an anthrax attack. The mathematical modeling compels a conclusion that anthrax, as a WMD, may inflict unquantifiable human suffering.

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