



Science and Technology Expert Partnership

Mathematical Modeling of the Spread of Selected Bioterrorism Agents —*Summary of an Open Conference*

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An Introductory Note

In the current international climate, there is considerable concern regarding bioterrorism, with attention directed toward the dispersion and spread of bioterrorism agents by a variety of mechanisms.

To address this and many other areas of concern to the national security, the STEP (Science & Technology Expert Partnership) program was developed as a National Intelligence Council (NIC) and Scientific & Technical Intelligence Committee (STIC) initiative to bring together government and national experts. This STEP activity was suggested by Dr. Lawrence Gershwin, National Intelligence Officer for Science and Technology, and was overseen by Dr. James Kvach, Chief Scientist of the Armed Forces Medical Intelligence Center (AFMIC) of the Defense Intelligence Agency (DIA). DIA/AFMIC is a member of the Intelligence Community (IC) and a crucial element of the Department of Defense's (DoD) force protection planning. In addition, Dr. Ellis McKenzie of the NIH and Dr. Alfred Steinberg of MITRE collaborated in inviting speakers, finalizing the program, and in co-chairing the conference. In order to focus the meeting, only a few bioterrorism agents were considered. It is anticipated that future conferences will address additional bioterrorism agents, including animal and plant pathogens.

This report was prepared by Alfred D. Steinberg, M.D., The MITRE Corporation, for the Scientific & Technical Intelligence Committee. Comments and queries are welcome and may be directed to Dr. James Kvach, Chief Scientist, Armed Forces Medical Intelligence Center (301) 619-7511.

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Summary

Models clarify thinking, provide a mechanism for asking important questions, and assist policy-makers in their decision-making and crisis management. One important aspect of model development is to identify the few critical parameters that have the greatest effect on the outcome. Values for these parameters (herein called “drivers”) need to be refined. This is an iterative process in which the models should become progressively more useful as additional data become available, important parameters are refined, and dispersion/spread models become more sophisticated.

Mathematical modeling of the spread of bioterrorism agents is a developing field. Although considerable effort has been expended to create relevant models, much more research and development work is required. Many of the variables needed for models are still not well-understood. Some of these may not even be well-approximated in some current models.

Microbial agents which spread person-to-person, such as the smallpox virus, can give rise to an epidemic, whereas agents that affect only those individuals who are initially exposed, such as anthrax spores, cannot. For agents that are contagious, the number of secondary individuals that each initially infected person subsequently infects (termed the R_0) is of critical importance in predicting the rapidity and breadth of the spread of an outbreak, and the public health measures needed to contain it.

From the models presented at this conference, it is clear that a single release of anthrax spores, which do not spread person-to-person, can cause large numbers of fatalities but not a national or international epidemic. An attack with an agent that is passed person-to-person, such as smallpox, can potentially cause a nation-wide epidemic and possibly even a world-wide crisis, requiring early detection, vaccination, and quarantine if it is to be controlled.

Short Statement of the Problem

In order for the US Intelligence Community (IC) and the policymakers it serves, to be better prepared to deal with national or international acts of terrorism, we need to understand the role that mathematical modeling of the spread and/or dispersion of bioterrorism agents might play in crisis management and public health decision-making. The purpose of this

conference was to determine the baseline ability of mathematical modeling to forecast the local, national, or international spread of an infectious disease due to an act of bioterrorism.

Findings and Forecasts

General:

1. Mathematical modeling can be an important tool to: sharpen understanding of fundamental processes, compare alternative policies and interventions, help to make decisions, provide a guide for training exercises and scenario development, assist risk assessment, aid forensic analysis, and predict future trends.
2. Decision-oriented models can be of great help in preparing for, and responding to, bioterrorism events much as they are in business, engineering, war, and other fields.
3. Models are tools to assist—not replace—critical thinking and to help in deciding which questions are most important.
4. There is inadequate support in the U.S. for the development and testing of mathematical and computational models for forecasting the spread of infectious diseases.
5. Mathematical modeling of the spread of infectious diseases has not yet become a mature discipline.
6. Several models have been developed that describe aspects of the spread and/or dispersion of microorganisms that could be used by terrorists. These models can provide useful information to policymakers and crisis managers.
7. Few policy-level consumers of bioterrorism models are well-informed about models, modelers, or the modeling process.
8. Modeling for each microorganism requires values/assumptions for that agent as well as other factors, including details of initial release and population at risk.
9. Agents which can be readily passed person-to-person have the greatest potential for national or international spread.
10. There are insufficient data to support various aspects of mathematical modeling research and development.
11. Identifying the few critical parameters (no more than 3-5) is an important aspect of model development.
12. Future work should include refinement of the values for these critical parameters.
13. The basic reproductive ratio (R_0), which describes the potential for a communicable disease to spread, is a critical parameter and should be estimated for all contagious human and animal diseases with bioterrorist potential. A $R_0 > 1$

allows an infectious disease to spread in a population, whereas an $R_0 < 1$ is associated with diseases that die out.

14. No two epidemics are identical. A R_0 from a prior disease outbreak may not accurately describe a new event with a similar organism.

Findings for Smallpox

1. Smallpox is a contagious disease with the potential for causing a world-wide pandemic.
2. Smallpox spreads as a result of person-to-person exposure, resulting in secondary and tertiary cases (in contrast to anthrax, which is not passed that way).
3. A high R_0 for smallpox (the number of individuals an infected individual will in turn infect) would predict much faster spread with greater likelihood of a difficult-to-control epidemic than for a lower R_0 .
4. There is disagreement regarding the proper R_0 for smallpox models.
5. Some smallpox models assume uniform mixing of the population whereas others assume that infected individuals will expose specific contacts with whom they have had “face-to-face” interactions during their contagious period. This difference is important in predicting outcome and in directing public health measures.
6. There is disagreement regarding the value of vaccinating contacts of infected individuals versus vaccination of the general population. Models that incorporate uniform mixing suggest mass vaccination whereas models that stress infection of contacts suggest vaccination of contacts for control.
7. Smallpox models suggest that delaying vaccination programs is very undesirable because there is a significant increase in casualties for each day of delay.
8. Quarantine reduces fatalities and helps to bring an epidemic under control in the models in which it was examined.
9. Quarantine and vaccination for smallpox outbreak control are superior to employing only one or the other.

Findings for Anthrax

1. Inhalation anthrax can occur after spores are inhaled, but infection is not passed person-to-person.
2. Although inhalation of 8,000 spores is considered to be the LD50 for anthrax in humans, the anthrax dose-response curve is broad, suggesting that the LD5 or LD10 might be substantially less. Indeed, two models predicted that between 5%

and 10% of individuals exposed to somewhat less than 200 spores would die from anthrax.

3. The number of casualties after an anthrax release could be markedly reduced if evidence of the anthrax release is determined immediately.
4. For an agent with a relatively high infectious dose such as anthrax, meteorological conditions may be a critical parameter in determining the number of casualties.

Findings for Plague and Tularemia

1. The microorganisms that cause plague and tularemia are more susceptible to atmospheric decay than are anthrax spores.
2. For an agent with a low infectious doses, such as tularemia, unstable meteorological conditions can lead to wider spread of the agent and worse consequences.
3. For both tularemia and plague, evidence of a release prior to clinical and laboratory diagnosis is critical to preventing large numbers of fatalities.
4. Quarantine would assist in reducing secondary spread of pneumonic plague.

Findings for Foot and Mouth Disease (FMD)

An epidemic was simulated for a portion of California based upon conditions believed to exist currently for USDA-mandated diagnosis and control of FMD.

The result suggested that much faster diagnostic techniques could play a critical role in disease control.

Pre-emptive ring slaughter was estimated to be more costly and less effective than pre-emptive slaughter of only the highest risk herds surrounding an infected herd.

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Purpose

The purpose of the Conference was to determine the baseline capability of mathematical modeling to predict the spread of pathogenic microorganisms used as bioterrorism agents.

Background

Mathematical modeling has the potential to assist in government planning for, and crisis management of, bioterrorism events. Indeed, modeling is well-suited to understanding what is known about the dispersion and/or spread of pathogenic microorganisms used as bioterrorism agents and to highlighting areas where additional information or work is needed.

This conference was arranged by The MITRE Corporation for the STIC as part of the STEP program. This is the third in a series of scientific programs to advance state-of-the-art knowledge. The first was held in September 2000, and the topic was mathematical modeling of infectious diseases. The second, held in September 2001, was on the future capabilities of genomics and proteomics by the year 2012.

The first of these modeling conferences concluded the following:

The field of modeling of the spread of various infectious diseases or forecasting conditions suitable for infectious disease outbreaks is still in its scientific infancy.

Modeling standards must be established.

Modeling of infectious disease epidemiology should be multidisciplinary, and include infectious disease experts, immunologists, modelers, statisticians, and epidemiologists.

Such modeling requires good data or superb assumptions, which must be easily testable.

If more than one group models a disease, resolving the bases for differences may allow the field to move forward. Without such resolution, users of modeling information may develop a lack of confidence in all models and their results.

Combining relevant portions of two different models may provide synergy.

It may be desirable for non-linear systems to be used as "expert systems" by non-modeler users to avoid an excess of parameters.

There is a great difference between diseases that are transmissible from one human to another and those in which the human is a "dead end" host. The modeling of these is very different in the details of the parameters used.

The best models allow reasonable conclusions that could be utilized by non-modelers, for example, epidemiologists and policy makers.

It is relatively easy to generate models, but validating them is a problem. Making the models predictive is especially difficult.

Models can be iterative, and predictive models, even when incomplete, are useful.

Models are able to tell what is known, the relative importance of different factors and, where we do not know enough, which information may foster improvement of the models.

This second conference on modeling of infectious diseases brought together experts in the areas of mathematical modeling of selected bioterrorism agents, including the causative organisms of anthrax, smallpox, plague, and foot and mouth disease. The experts were associated with government, academia, and industry. The conference included healthy debate and provided insights into the strengths and limitations of different approaches to mathematical modeling of the spread of infectious diseases.