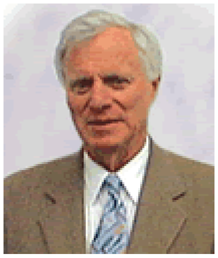
Early Warning and Remediation: Minimizing the Threat of Bioterrorism

Philip J. Wyatt
Chief Executive Officer, Wyatt Technology Corporation
April 2002



Philip J. Wyatt is the Chief Executive Officer of Wyatt Technology Corporation. Dr. Wyatt received his undergraduate education in liberal arts, physics and mathematics at the University of Chicago, and Christ's College, Cambridge. His graduate education was completed at the University of Illinois (M.S.) and the Florida State University (Ph.D.). The author of more than fifty articles, Dr. Wyatt has co-authored three textbooks, and was one of fifteen finalists for this country's first Scientist-Astronaut Selection Program. He is a Fellow of the American Physical Society and the Optical Society of America, and has had over thirty foreign and domestic patents issued relating to laser light scattering.

Background

The focus of this paper concerns the early detection of biological agents being used as weapons of "mass destruction"—that is, able to produce thousands of casualties as a consequence of a single attack. More recent "targeted" attacks, such as those delivered by mail, are treated as localized attacks for which early warnings are also sought. A new problem created by such localized attacks concerns the detection and remediation of residues following such attacks and the means by which they may be removed or otherwise rendered harmless. This topic is discussed later and may well represent the biological equivalent of residual radioactivity following a nuclear attack.

With the 11 September 2001 cataclysmic terrorist attacks on New York City and the Pentagon, the use of biological agents attracted renewed attention as a possible *next* means for a terrorist attack. With the 2001 plethora of anthrax spore incidents, it appears that such attacks have started already.

The generally accepted "best mode" for delivering a biological weapon has been by means of a dispersed aerosol cloud,[1] the colorless and odorless constituents of which are inhaled by an unprepared population. More recently, anthrax spores have been disseminated using the mail to deliver envelopes that, when opened, release small "puffs" of weaponized spores. While the envelope delivery results in a localized attack affecting at most some tens of individuals, employment of a dispersed aerosol cloud, if it works, appears to be the most certain means of inflicting catastrophic consequences on the targeted population. The only way either of these results may be prevented or reduced significantly is through an early warning to the targeted populations. Without such warning, there is little likelihood that the exact nature of the disease or toxicant will be known until a large fraction of the compromised population begins to show pathological symptoms. In addition, only by such warnings would local populations know when to deploy protective masks and enter protective shelters (were such available) or, in the case of envelope delivery, leave the room. Even with the most ambitious of the current rapid diagnostic armamentaria available, such diagnoses may require several days for confirmation. The possibility remains extremely low that target populations will have sufficient triage capabilities, antibiotics (as required), or even antitoxins in sufficient quantities to treat those already affected. Were the attacked populations to receive an early warning of the threat together with details of the threat cloud or puff position and presumptive composition, the possibility of a successful attack might be reduced significantly. Indeed, were the target populations sufficiently prepared to take the necessary steps to prevent infection or inhalation of the cloud or puff constituents, the success of the attack could be so dramatically reduced as to make its initial deployment a somewhat useless exercise. A major disruption of civilian authority, even without physical casualties, still might be considered by the terrorist to have been a success. Proper training and preparation of potential target populations could ameliorate such consequences, however.

An unwarned population falling victim to such a bioterrorist attack, which introduces a virulent biological aerosol into a heavily populated area, might be almost as helpless to mitigate the situation as were the populations in Europe during the period of the Great Plague[2] of the mid–14th century. Besides the lack of adequate medicines and hospital facilities for the stricken, the psychological[3] and even the legal[4] consequences would be without historical parallel. "Biological Terrorism: Legal Measures for Preventing Catastrophe" by Barry Kellman is a well-written work that presents, among other things,[5] some of the unexpected legal impediments for a suitable and rapid response following such an attack. Many talks have been presented[6] concerning such scenarios and the great difficulties of coping with them. Invariably, medical supplies would be inadequate to treat the affected, and vaccines or other prophylactic materials would be too late and in quantities far too small to slow the propagation of disease and illness. Once again, were the targeted populations given early warning of the in-progress attack, casualties could be reduced significantly and perhaps be avoided altogether.

Early in 1999, the Institute of Medicine, in collaboration with the Commission on Life Sciences of the National Research Council, released a report,[7] *Chemical and Biological Terrorism: Research and Development to Improve Civilian Medical Response*. This report (the "National Academies report") was produced by the Committee on R & D Needs for Improving Civilian Medical Response to Chemical and Biological Terrorism Incidents, which was appointed by the Institute of Medicine and the Commission on Life Sciences at the request of the Office of Emergency Preparedness (Department of Health and Human Services). The committee was asked to

(1) collect and assess existing research, development, and technology information on detecting potential chemical and biological agents and protecting and treating both the targets of attack and health care providers, and

(2) provide specific recommendations for priority research and development

The National Academies report presents a timely picture of the country's ongoing research and development efforts in this area together with recommendations for future research programs with the objective of minimizing casualties from such terrorist attacks. The report also provides extensive inventories of chemical and biological defense technology resources available in early 1999 as well as those expected for the near term following. Although the committee considered both chemical and biological threats, the focus of this article is primarily biological attacks—that is, those involving the release of pathogenic microorganisms as well as a variety of significant toxins produced by microorganisms and plants. Responding to the question of an early-warning system, the National Academies report states, at its onset (in the Executive Summary):

> Real-time detection and measurement of biological agents in the environment is more daunting [than the measurement of chemical agents], even for the military, because of the number of potential agents to be distinguished, the complex nature of the agents themselves, the myriad of similar microorganisms that are always present in the environment, and the impracticality of providing real time, continuous monitoring at even a fraction of the sites of potential concern. Few if any civilian organizations

currently have, or can easily obtain, even a rudimentary capability in this area.

Before discussing this conclusion, let us review briefly some of the key elements expected of a real-time early-warning system.

The agents[8, 9] of greatest interest for bioterrorists include endospores (for example, from *Bacillus anthracis*), lyophilized or otherwise viable bacteria (for example, *Yersinia pestis* and *Francisella tularensis*), viruses (for example, smallpox [variola]), and toxins (for example, botulinum [from *Clostridium botulinum*]). The symptoms of many of the diseases associated with these agents are rarely seen when the mode of infection is by inhalation; thus the diseases are often difficult for typical hospital staffs to diagnose properly. In addition, it is relatively easy to modify the antibiotic susceptibilities of the selected bacterial agents.[10] Thus, providing huge stockpiles of antibiotic agents[11] suitable for treatment of the most likely expected bioweapons might well be a waste of effort. The leading candidate for an aerosol deployment—anthrax spores—is an even more unusual source of infection because the resulting illness must be recognized and treated with large quantities of the drugs of choice *before* symptoms appear. Yet, as previously mentioned, the early symptoms of an inhalation anthrax infection are easily confused with a wide variety of viral, bacterial, and fungal infections, so early diagnosis may be further delayed. Once symptoms appear, inhalation anthrax is fatal[12] irrespective of the treatment: the toxin overwhelms the victim. Until recently, there has been great emphasis on vaccination,[13, 14] especially of the armed forces, to protect a targeted population against anthrax. Such vaccinations have their drawbacks, yet they have now become available for civilian populations. A recent discovery by Bret R. Sellman, Michael Mourez, R. John Collier[15] suggests that the administration of mutant protective antigen to individuals infected with anthrax could provide protection even at an advanced stage of the disease. Most important, protective antigen itself, several of the mutations of which have been shown to be an effective antitoxin, is already produced in great quantities during the manufacture of anthrax vaccine. Thus, there may be a means on the horizon by which, no matter how manipulated the antibiotic sensitivity of the anthrax weapon, a suitable post-infection antitoxin may be readily available, making this weapon of choice far less attractive. Since large quantities of toxins are released rather suddenly in actual infections, it remains to be seen whether mutant protective antigen would be effective for such advanced cases of infection. Much work must be completed before mutant protective antigen administration can be considered safe for human use. Quantitative dose levels must be established, and the possibility of promiscuous binding to various cell types must be explored in detail.

Why Early Warning?

The importance of early warning of a bioterrorist attack cannot be overemphasized. Indeed, the simple expedient of providing some means for protecting the respiratory system ("masking up") from the inhalation of the terrorist-introduced aerosol could be expected to provide sufficient protection until the threat cloud had passed. Given a sufficiently early warning of an imminent aerosol attack, simply returning to one's home, closing all windows, covering the entire body with even a wet sheet, and remaining generally inactive would be sufficient actions to protect the vast majority of the targeted population. For small puff deliveries, the immediate protection of the respiratory system using a handkerchief, for example, followed by the immediate departure from the targeted area (room) would suffice. These would certainly be reasonable courses of action until a satisfactory decontamination effort by the local authorities had occurred, and it could be confirmed that it was safe to resume normal activity. The actual means by which such early warnings may be provided to any at-risk population, together with an adequate education program to ensure a clear understanding of the risks and measures required to overcome the dangers posed by such bioterrorist attacks, become more clearly understood once the nature of the aerosol threat itself is examined. Indeed, once such early-warning systems have been deployed, the likelihood of a biological attack with a successful outcome becomes very small. In order that the consequences of such an attack be minimized, the development and deployment of such an early-warning system becomes the highest priority to discourage the implementation of bioterrorism *ab initio*.

Would a deployed early-warning system affect the premise that bioterrorism presents a significant danger? If so, have earlier or current technological achievements (such as the discovery by Sellman, Mourez, and Collier) rendered the perceived threat far smaller? In recent years, the threat of terrorist acts involving the use of biological agents has taken on additional importance. With a general increase of terrorist acts throughout the world,[16] it is reasoned that attacks using biological agents could be initiated at relatively low cost and with minimal technological skills by rogue states or fringe groups. The deliveries of anthrax spores via mail emphatically confirm this conclusion. Arguments that such acts must be prevented or, at worst, their consequences minimized have resulted in significant funding for those pursuing this premise. Conferences have been organized,[17] study centers created,[18] articles warning of the associated perils published in unprecedented quantities,[19] and significant federal spending initiated to fund a great many of the concepts proposed to ameliorate the threat. The U.S. government had spent hundreds of millions of dollars over the previous 50 years studying many of the same areas, but this work has been generally ignored in the rush to justify the newly authorized funding by a concerned Congress. Many of the organizations enjoying such federal largesse rarely refer to each other's accomplishments in the course of preparing their own papers and reports. Even mention of the National Academies report is rarely found among their references despite the report's exhaustive presentation. Regrettably, these organizations seem to fear that such citations might give the impression that the uncited other group would share their capabilities (and funding).

The Department of Defense has directed a large fraction of federal funds toward developing early detection and warning systems.[20, 21] According to the National Academies report, most of the funding for biodetection devices comes from the Department of Defense (56%), with 18% from commercial ventures. The Department of Energy, the Food and Drug Administration, NASA, and the Tactical Standards Working Group account for the remaining 26%. Of the 73 devices[22] under development in early 1999, only 6 were commercially available; 29 of the remaining 67 were in the field-testing stage, and 38 were still in the laboratory. The National Academies report placed considerable emphasis on the fact that the value of all the various military developments diminishes considerably when applied to "the most probable civilian terrorism situations, in which the enemy, the agent, the time, and the place of attack are unknown." Substantial efforts have been directed to exploring means for the early identification of the threat agents and the early treatment of victims,[23] yet many of these ongoing programs are very similar to those supported 30 to 40 years earlier,[24, 25] and little note is made of these earlier attempts and their results. In 1963, for example, the government spent $158 million in the area of biological warfare defense,[26] a figure comparable to the $1.4 billion currently appropriated for defense against all weapons of mass destruction. Although virtually all reports written during that period are now accessible under the Freedom of Information Act (assuming they have not been destroyed), they are difficult to obtain, and few current programs are aware of, or have any interest in, this work. Yet it should be emphasized that in those years, the government laboratories were staffed by many of the brightest and innovative scientists.[27] To conduct their biological research, these scientists may not have had all the tools now available, but they often made up for these shortcomings by their remarkable ingenuity as well as their focus on the problem rather than strategies for obtaining federal funding.

Most agencies currently supporting biodefense research (primarily the Department of Defense) seem to believe that an early-warning system producing a false positive result is of far greater significance than the possibility that among such false positives will be a true positive. Particular emphasis[28, 29] has been directed toward avoiding a false positive alarm because of the panic that would be expected in a representative civilian population (as if there would be a lesser panic among the same group having been warned of a true attack!). The importance of developing detection and early-warning systems absent any false positive components is taken for granted without any memory, for example, of the air raids on civilian populations during the Second World War. All threats of imminent danger are always perceived with panic, but there were few complaints directed toward the "authorities" following an "all clear" announcement of a false positive air attack. The public reaction was generally grateful, despite the discomfort associated with entering and remaining in an air raid shelter for the period of the threat. Apparently, a similar civilian reaction is discounted for a bioterrorist attack. Considerable attention[30] has been devoted to the need for suitable education of all potential population targets of bioterrorism, though, for the most part, this has been more theoretical than practical. Still, compared to the 1950s, for example, when this country was heavily involved in the development of biological weapons, there has been very little attention given to alerting the public to these dangers. In earlier times, the Department of Health, Education and Welfare published pamphlets[31] intended to assuage civilian fears of such attacks and to explain precautions that might be taken for protection.

Accordingly, an early-warning system with a reasonably high probability of calling true positive events would be invaluable and certainly *the method of choice* in confronting the bioterrorist threat. Unfortunately, the National Academies report, as earlier quoted, all but abandoned such a concept. The current emphasis of virtually all government spokespersons relates to areas of civilian, policymaker, and medical participation and action. Certainly, this emphasis alone will help to ameliorate the elements of panic associated with such an attack and help minimize the consequences during an attack. Other elements stressed in the National Academies report were the development of adequate care delivery systems; coordination of police, military, and civilian direction following an attack; and development of new tools for medical management. The last item includes the ongoing needs for better antibiotics, better vaccines and related preventive medical care, and a national stockpile of drugs and pharmaceutical products.

An early-warning system still remains the paramount objective for defense against an attack based on the delivery of a dangerous biological agent by aerosol means. The Preparedness Against Domestic Terrorism Act of 2001[32] emphasized in "Findings and Purposes" (§2) that "the President should strengthen Federal interagency emergency planning by the Federal Emergency Management Agency and other appropriate Federal, State, and local agencies for development of a capability for early detection and warning of and response to potential domestic terrorist attacks involving weapons of mass destruction." The detection and unequivocal determination that a specific agent known to be a biological hazard had been introduced and was present would be *sufficient* cause to initiate a warning alarm. But is such confirmation *necessary* to conclude that a biological attack has occurred? The demand, by some quarters, that a biological aerosol threat be detected with a minimal probability of a false positive result seems to suggest that such definitive identification is a characteristic that is *both* a necessary and a sufficient property of a suitable early-warning system. Yet many elements associated with an aerosol delivery might confirm to a high level of certainty that an attack had occurred, even without a definitive identification of the agent(s) employed. Furthermore, an unequivocal confirmation that a biological aerosol threat had been inserted into a community or facility or room helps little in establishing the most suitable means for initiating and distributing an alarm. Certainly the point of insertion of the threat or, at the very least, its current position should be determined. In addition, the extent and movement of the threat cloud must be known for suitable warnings to be made for the benefit of the threatened target. Indeed, knowledge of the instantaneous location and projected appearance of each *element* of the threatening aerosol would be invaluable in providing maximum warning time for the subsequent protection of the targeted area. The effectiveness of an early-warning system, therefore, will depend critically upon the ancillary information available at the time of, and immediately following, the attack. Not only must all elements of the threat cloud be tracked and monitored, but the local meteorological conditions must be known, as well as how they would affect the cloud's motion and extent. Integration of these conditions into tracking software[33] would ensure that the alarm and warning systems would perform optimally. For puffs delivered to specific rooms or contained locations, the mere confirmation of their presence is sufficient cause for an immediate evacuation followed by containment of the affected facility.

Features of an Aerosol Threat

There appear to be few avenues for implementing such an ambitious early-warning system. To explore the possibilities that exist, we should examine the characteristics of a biological aerosol threat that, in turn, will define the most propitious elements of an early-warning system. Table 1 lists the important properties and characteristics of a potentially dangerous aerosol cloud. Important operating features of an early-warning system will flow from the discussions following each property described. In addition, it should be noted that some properties listed play major roles in *diminishing* the aerosol cloud's effectiveness and, thereby, the probability of a "successful" bioterrorist attack. An early warning of a more localized envelope-delivered puff, on the other hand, should be more easily provided by means of a localized detector. These latter implementations will be discussed later. For the present, we shall focus on the more potent weapon of mass destruction: a dispersed aerosol cloud. Many of the cloud properties will have corresponding puff properties, though on a far smaller scale.

Table 1. Hazardous aerosol cloud properties

Properties	Discussion
1. The cloud appears within a short timeframe.	The aerosol was not present for a significant period of time before it was detected. This suggests that monitoring must be *continuous* throughout any regions considered potential targets.
2. The constituents of the cloud are similar.	The basic objective of a terrorist-deployed aerosol is to inflict biological damage or chemical damage on an unsuspecting population. To make efficient use of the delivery mechanism *per se*, the particles introduced will be very similar in structure and function. Thus an aerosol being used to deliver anthrax spores will comprise individual spores or weaponized variants. The vast majority of such particles will be of one or, at best, a few distinct forms and structures, which in turn may include more than one agent—for example, both spores and a toxin.
3. The constituents of the cloud will be quite different from those that occur naturally.	None of the aerosol particles of choice are found in a natural airborne environment. Respirable biological particulates are only rarely found in nature. They do not appear by accident in large quantities. Two studies[34] of ambient bacterial levels confirmed the fact that they are very low. The three-year Swedish study in the 1970s found that concentrations of airborne bacteria in a typical city street varied between 100 and 4,000 per cubic meter. Of these, over 50% were attached to particles larger than 8 µm. The highest levels reported *indoors* in a 2001 study of airborne bacterial levels in Hong Kong shopping malls exceeded 1,000 per cubic meter. So even in this extreme case, no more than a few bacteria *per liter* occur naturally indoors in the presence of significant human numbers and movement.
4. In ambient air, each constituent of the cloud falls very slowly.	For simplicity, consider a cloud comprising *B. anthracis* spores, with each such spore characterized simply as a sphere of a diameter of about 1.5 ?m and unit specific gravity. Applying Stokes' law under ambient atmospheric conditions at a temperature of 25 (C), we find that (absent any wind or convective forces) it will require over 3.5 hours for the spore to fall just one meter! Interestingly, for envelope-delivered puffs, these

	properties ensure that the local area of introduction will remain hazardous for a great length of time. This slow fallout rate of micrometer-size particles is well known and, for example, responsible for the effectiveness of military smoke screens and their stability over relatively long periods of time. On the other hand, this slow descent suggests that aerosol deployment from a low-flying airplane (a popular delivery concept[35]) could be quite difficult if the targeted population is to be reached at all.
5. The concentrations of the aerosol particulates will be very great compared to the concentrations of the naturally occurring aerosols.	Because the aerosol cloud is introduced to attack the targeted population through the vehicle of a pulmonary infection route, the ambient levels required to produce infection within a relatively short time will be elevated significantly above ambient aerosol levels. (See the discussions that follow.)
6. The aerosol cloud, once delivered, will spread.	Although diffusion of the cloud constituents in ambient, still air is very slow, under most naturally present atmospheric conditions such as wind and temperature gradients, the cloud boundaries and volume will expand, often quite rapidly. Even in an enclosure containing a puff release, the presence of eddies created by air-conditioning systems or human movement will aid in the dispersal of the puff.
7. The particulate concentrations will be extremely heterogeneous.	Since the aerosol particle diffusion in an ambient atmosphere is negligible (see item 4 above), the initial concentrations within the injected cloud will be affected discontinuously by local vortices, wind gusts and similar atmospheric inhomogeneities, buildings, and other obstacles. Indeed, the boundaries of the inserted cloud would represent well-defined regions of concentration discontinuities. The Sverdlosk release or accident[36] of 1979, deduced to have been caused by less than 1 gm of spores, resulted in at least 68 human and numerous animal fatalities. Calculation of the initial distribution and spreading of the released anthrax aerosol was based on a Gaussian plume model with a set of estimated initial conditions. Although this model did not describe density discontinuities, it correlated well with the tabulated mortalities. It seems likely on the basis of new types of mathematical analyses[37, 38] that the spore concentrations within the infectious elements or cells of the released puff remained discontinuous as these elements were driven by slight winds through well-localized regions adjacent to the source facility. The concentration gradients transverse to the wind direction appeared to be and remained large.
8. Particulate concentrations within the delivered aerosol will vary with time.	Because of the spreading of the cloud as it passes through the target region, the particulate concentrations present at any localized region in space will vary with time according to atmospheric conditions (winds, temperature gradients, etc.) and physical barriers.
9. In ambient air, biological particles dispersed within a meter of the ground will not	Once spores, bacterial cells, and biological droplets reach the ground, they generally adhere to the soil or to larger, non-respirable particles and remain there. Small eddies

be particularly effective.	may tend to re-suspend them, but the closer they approach the ground, the smaller the probability that they can be dislodged.
10. To be most effective, the aerosol cloud must be introduced at or reach an altitude compatible with the target population's inhaling the constituents.	If local winds or atmospheric disturbances carry off or otherwise remove (for example, by means of rain) the constituents before they are breathed, the constituents are ineffective. It may be difficult to localize a delivery to such a low altitude without risking detection. This is not true of envelope-delivered puffs, whereby delivery is almost perfect.
11. The constituents of the cloud will be proteinaceous.	Lyophilized bacterial cells, bacterial spores, botulinum and other toxins, and virus-containing respirable particulates are all expected to have protein components. Most naturally occurring aerosol particles do not.
12. The release of a bioaerosol by terrorists intent on causing maximum effects most certainly would be initiated under nearly pristine atmospheric conditions with, at most, a slight breeze moving toward the intended target area. The release of ultraviolet-sensitive aerosols probably would be at night. Labile organisms would require release at selected times when temperature extremes could be avoided.	Releasing such agents in the midst of a rainstorm or severe atmospheric disturbance would achieve very little, as the agent constituents themselves would be cleared or removed rapidly from their intended target. Releases during exceptionally high background aerosol levels (of dust or pollen, for example) will be avoided to improve the possibility of a successful deployment of the threat agents, since the presence of these natural background aerosols always will play some role in scavenging or scrubbing by adsorption the newly introduced biological particles. Protecting the released aerosol particles from deleterious effects of the sun's ultraviolet radiation or temperature extremes of daytime heat would restrict further the window of opportunity for a successful release. Releases under such good conditions, on the other hand, improve the probability of early *detection*. Spores are somewhat less susceptible to ultraviolet or temperature extremes, but weaponizing may well protect other bioaerosols as well. The closed environments of a room or confined space wherein puffs may be envelope-delivered are well within the class of pristine.

Elements of an Early-Warning System

With the properties of the threat cloud and conditions for its introduction as listed in Table 1, the important operating capabilities of the early-warning system may be delineated further. Thus the system should be capable of detecting and (as required) identifying the following:

1. The location, time, and spatial extent of the initial aerosol cloud at the moment of introduction (within a room or closed environment, detection of the initial time of release is essential)

2. The subsequent and continuing dynamics of the aerosol cloud, including the composition and movement of all of its constituents

3. The preliminary classification of the physical characteristics of the individual aerosol particles introduced; such classification should include the types of particles characterized, such as bacterial spores, bacterial cells, liquid droplets, and virus-sustaining droplets

4. The particle size distributions and changes of these distributions in time (if any) of each classified aerosol particle present

5. The continuous concentrations of the classified aerosol particles at all regions occupied by the cloud and their spatial correlations with physical structures (for example, buildings) present (if any)

In addition to these five requirements for a system of identification and detection, the system must play an active role by being capable of notifying the local population of the impending danger posed by the cloud, its estimated location, and the timeframe for taking protective action. Finally, the early-warning system must be automated with very little user intervention.[39] Once again; releases of puffs via envelope-delivery means in highly localized regions such as rooms should be more easily detected. Consider now the available devices that might be important elements of such a system.

Extant Solutions

By means of generous funding, the government continues to support the development of some interesting "solutions" to address the problem of early detection with unambiguous identification. For the most part, they are slow and costly. Many are impractical, and such impracticality was demonstrated many years earlier in the similar government programs referenced above. One of the approaches most frequently revisited includes variations of lidar techniques[40, 41] using lasers, often in the ultraviolet, as the optical analog of conventional radar. The objective of these systems is so-called "stand-off" detection whereby the threat clouds may be detected, classified, and identified before they reach their intended target. As with other types of radar interrogation, until the laser beam sweeps a particular region, that region will remain unmonitored. The placement of such systems can seriously impede their ability to examine certain regions, and the possibility always exists that the threat cloud will be released in a region inaccessible to the lidar beam. The value of an early detection determination of the information returned by a lidar signal remains uncertain because such signals cannot be correlated unambiguously to an explicit terrorist-introduced aerosol.

A complementary approach that examines the local region in which the system is located (so-called "point source" detection) is the Biological Integrated Detection System (BIDS) developed by the Department of Defense. This mobile system,[42, 43] intended for use primarily by military ground forces, is activated by an alarm from an aerodynamic particle sizer tuned to detect the appearance of aerosol particles in the respirable range of 1 μm to 10 μm. Following detection, such particles are collected in a liquid and then subjected to specificity tests, including selected enzyme-linked, immuno-sorbent array assays, a pH sensor, several specific DNA stains, a chemical mass spectrometer, and a miniaturized flow cytometer. The resultant set of data is assumed sufficient to identify the threat specifically while avoiding a false positive result. The time required for a complete analysis can be many hours or more. In addition, the BIDS must be placed at a single collection site and is limited, therefore, to a very small monitoring region. (The equipment is far too large to place in closed areas such as rooms!) In essence, BIDS is a rapid-response mobile microbiology laboratory equipped with the very latest and modern testing and analytical equipment.

The particle number concentration variations within the aerosol cloud itself are not easily describable. The particle concentration would be little changed in an ambient environment because the particles would diffuse and/or fall so slowly (see Table 1, feature 4). Only winds, local atmospheric instabilities (eddies), and thermal gradients would affect the cloud's position and mixing with its surroundings. Assume that a swath 2 km long, 10 m deep, and 20 m wide of viable *Bacillus anthracis* spores has been released upwind of a targeted area. An airplane or even a land vehicle could produce this cloud. Once again, as cloud constituents reach the ground or come to rest within the boundary layer of laminar flow near buildings and other solid obstacles, they may adhere and, effectively, be removed. Presumably, the remaining cloud will be pushed by winds, eddies, and thermal gradients through the targeted region and be diluted in a very unpredictable and random manner by means of the obstacles (for example, buildings) about which it flows, as well as local meteorological conditions. Taking the dimensions of a typical spore at about 1.4 μm in length by 0.9 μm in diameter and assuming unit density, the mass of a single spore would be about 8.9 x $10^{-13\text{ gm}}$. Using a figure from David Siegrist[44] of 10 kg to produce a nuclear-weapon-equivalent lethal release, we find that the number of spores is just 10^4/8.9 x $10^{-13\text{ gm}}$ = 1.12 x 10^{16}. Since the total volume released is 2 x 10^3 x 10 (20 = 4 x 10^5 m^3 = 4x10^{11} ml, the density at release of spores within this swath would be 1.12 x 10^{16}/ 4 x 10^{11} = 2.8 x 10^4 spores/ml. Taking a lethal (LD_{90}) pulmonary loading[45] of about 10^4 spores, a single breath from this swath of 1 liter will result in an immediate overload and subsequent death. Naturally, lower doses may kill some individuals, though the exact relation between an individual's physiological state and lethal dose is unknown. No children seem to have been affected at Sverdlovsk,[46] but this has not been explained.

Using O. G. Raabe's seminal compilation and study[47] of the deposition and clearing of inhaled aerosols, we can estimate the huge dilution factor of the original cloud that would ensure lethal inhalation by a targeted population. With a pulmonary tidal volume of 750 ml to 1450 ml, the deposition fraction in the deep lungs, for an active person breathing 15 times per minute by mouth, of particles inhaled with a size of *B. anthracis* spores is between 30% and 50%. For nasal breathing, on the other hand, the deposition fraction would fall to between 10% and 25%. Much slower, normal breathing of perhaps 10 breaths per minute would reduce these numbers further. Taking an average volume of 1,000 ml, a resting nasal inhalation rate of about 15 breaths per minute, and an exposure time of 1 hour, we find that the total volume inhaled is about 15 x 60 x 1,000 ml = 900 liters. If 10^4 spores are retained by the pulmonary cavity within this period and this represents 25% of the spores inhaled, then the minimal concentration needed to ensure a lethal dose inhaled and deposited in the deep lung within an hour is about /nobr>10^4/[1.8 x 10^6 x 0.25] = 0.022 = 2.2 x 10^{-2} spores/ml = 22 spores/liter! The original concentration deposited corresponded to 2.8 x 10^7 spores/liter, so that until the dilution of the initial cloud is increased by a factor greater than 2.8 x 10^7/22 = 1.27 x 10^6, the cloud will remain lethally toxic at a 1-hour exposure. As the volume of the initial swath was 4 x 10^5 m^3 = 4 x 10^{-4} km^3, the final extent of a lethal cloud could be as great as 4 x 1.27 x 10^2 » 500 km^3. Fortunately (?), the threat cloud will not experience a uniform expansion but will be subjected to the various dispersal mechanisms discussed earlier to yield a highly heterogeneous distribution. It might be reasoned that instead of releasing a small, highly concentrated volume such as that just described, the terrorist might reach a far greater population by releasing a much larger cloud achieved by greater dilution of the initial release. However, the release of such a huge cloud capable of maintaining 60-minute lethality would take considerably more time and increase significantly the likelihood of detection during deployment.

Envelope-delivered puffs, on the other hand, are particularly dangerous if undetected, because such puffs will generally be restricted to the room or area of release. There will be no strong winds or major atmospheric disturbances to sweep the threat away, and air-conditioning systems may rapidly establish a uniform distribution within the enclosure. Thus the effects of cumulative breathing will be of far greater importance than they might be out of doors. If the threat is not detected, the exposure of some individuals may be for many hours. Thus very low concentrations could be expected to produce lethal dose levels quite rapidly. At normal breathing of, say, 900 liters per hour, concentrations as low as 22 spores per liter could produce an LD_{90} within an hour! Early warning becomes an even more urgent issue for these "minor" releases.

The Integrated Early-Warning System

Among its most important recommendations, the National Academies report emphasized the continuing need for software developments that would "improve modeling of the environmental transport and fate" of the biological agents. It is not difficult to conclude from the above example, which again emphasizes the heterogeneous distributions expected of the deployed threat cloud, that the only effective means by which threatened populations may be provided with sufficient early warning is through the deployment of point-source detector stations *throughout all regions* where protection is sought. Real-time reporting by these stations is needed to provide the data required by the software models for early warning to the targeted populations. Each such detector must be capable of detecting the presence of an unusual aerosol, providing a presumptive or "best guess" identification (if such is available), monitoring as a function time the population of such aerosol particles in terms of their composition and number density, and continually updating the presumptive identification. But these are just the real-time detection features required of *each* detector station. In addition, each must be provided with networking capability to transmit the results of each measurement period to a central station for subsequent correlation, analysis, and prediction. An early function of the central station is to examine the data being collected and transmitted to it in terms of the hazardous aerosol cloud properties listed in Table 1. The degree to which the newly detected aerosol properties correlate with those listed in the table would allow for an earlier alarm warning of the potential threat even before more quantitative data had been collected. In a sense, the properties of Table 1 represent the forest, while the results of any single detector station corresponds to a tree. It must be the overall objective of the detector network to recognize early the aerosol *threat* (the forest) rather than focus on any single detector response (a tree). Only by such means will the system be able to provide adequate warnings to an unsuspecting population while initiating tracking and localized warnings of the terrorist threat. Naturally, the small puff release into a room or similar enclosure represents a very special case. On the one hand, such a limited region may have no detector station present and, therefore, no chance of early warning. However, if some rooms or regions do have detector stations linked to a central station, the detection by one or several single-room detector stations should result in a determination by the central station that the entire building or region may be threatened and thereby would produce an early-warning alarm.

The central station must process the data received from the detector stations to calculate the current spatial extent of the threat cloud and predict its future position and aerosol distribution. It must examine also the presumptive identifications transmitted by each reporting detector station and resolve any conflicting reports and identifications. The central station should be capable, as well, of directing specific detectors to change their sampling rates as well as to zero in on the detection of specific aerosol properties already confirmed as suspicious by other stations. On this basis, using the input data from vast arrays of detector stations, false positive alarms can be minimized significantly. A well-networked system of detector and central stations should provide all the information required of a meaningful early-warning system . However, associated with the network itself must be the adequate and suitable placement of the detector stations throughout the region explicitly selected for protection as well as peripheral regions through which threat aerosols may intrude.

Of the aerosol particles measured and classified by each detector station, there will exist always the possibility that the threat particles will represent a very small fraction of the particles processed. Ordinarily, if only a single detection station is in use, such associated events might be overlooked or discarded as most probably representative of an error due to the detector station itself. Because of the vast array of detector stations deployed for an early-warning system, such rare events will appear at other contiguous detector stations and, because the stations are linked and their measurements correlated, will effectively reinforce the conclusion that these small populations do indeed represent a real constituent of the sampled aerosol. Thus the ability to detect *and* classify very low fractional populations as they appear and are detected at successive stations is a critical requirement of an early-warning system . Equally important is the function of the central station linking a large set of detector stations. For localized releases in confined areas that may have only a single detection station, any delay in detection can result in a determination that the detected signals corresponded to an unlikely event. It is imperative that these single detectors have a high enough sampling rate to ensure detection at the earliest possible moment.

Having identified the general structure of an integrated early-warning system, the constituents of a typical detector station must be defined. A station must have small power requirements and be able to operate for many months, or even years, in a very wide range of physical environments with minimal requirements for service and maintenance. Each station must be self-diagnosing and capable of reporting any malfunction to the central station. As discussed previously, each station must be capable of both collecting data and processing them. Thus each must have both computer and memory means including both ROM and RAM elements. Interfaced with these elements would be suitable telecommunications components (a receiver/transmitter, antenna, power supply, small memory, etc.) to permit two-way data transfer between the station and the central station as well as enable reprogramming of each detector station by the central station. These properties, which are essential for the early defeat of most bioterrorist attacks, narrow the types of detector strategies that might be implemented using available technologies. Certainly all wet-chemistry detection methods are not practical, nor are so-called one-shot devices such as biochips. Methods relying on collection and subsequent wet-chemistry analyses such as fluorescent antibody staining techniques are impractical for such deployment. Methods incorporating mass spectrometers and the preparation apparatus for such measurements are equally impractical. Methods requiring the pre-seeding of protected areas with a broad range of antibodies are impractical,[48] and methods based upon constant airborne or other stand-off approaches would be incapable of protecting arbitrary population centers selected by bioterrorists for their target.

No matter what detection method is employed to provide for early warning, eventually the agent will be so diluted that it may no longer be detectable—such as when the initially inserted biological agent cloud (puff) becomes diluted by the atmospheric mixing and physical obstacles. Such limits of detection will depend on many factors, including the sensitivity of the detection system, interfering background particulates with signatures that overwhelm or confuse the detection system, and the local concentration of the inserted agent. Theoretically, some agents may continue to be dangerous (disease threatening) even at extremely low concentrations. In the example presented concerning the introduction into the atmosphere of a swath of anthrax spores, at a constant concentration of only 22 spores per liter, an infective and potentially lethal dose could be inhaled and deposited after just one hour of breathing. Even lower residual levels still may prove effective after many additional hours of cumulative inhalation. Neglecting background particles that may interfere with the detection of the targeted aerosol particles, at some low concentration the collection and subsequent detection technique employed will miss the target aerosol particles entirely and report none present. This fact adds urgency to the need to detect the threat at the earliest possible moment and at a location as close to the release location as possible. Such early detection, combined with further development of software capable of accurate prediction of the cloud concentration as a function of position, will permit subsequent notice to the attacked population of an “all clear, safe to come out” condition.

The concept of examining the aerosol particles one at a time by various analytical means has always been attractive. For the BIDS laboratory described earlier, the collected particles, once pre-processed, are examined in a flow cytometer. For such examination, the particles may be stained and their fluorescence spectra examined as they pass through an intense beam radiated by a laser. The measurements thus occur *in vitro* rather than in a more desirable *in situ* setting. Some work has been reported on single-particle *in situ* measurements by which the presence of biological particles may be confirmed by detecting their characteristic fluorescence.[49]

A great amount of effort is being directed to the development of biochips, immuno–polymerase chain-reaction methods, genetic sequencing, SMART tickets, biological warfare tickets, single-particle fluorescence counters, ligand-based probes, fluorescence-based transduction, and other devices and techniques to detect specific markers characteristic of various classes and types of potential biological agents.[50] Yet it is clearly evident that the biological aerosol constituents themselves are easily modified to deceive many such detectors. Indeed, it often may be possible to coat or otherwise modify individual aerosol particles with a wide variety of materials, making their biochemical identification even more difficult and time consuming. Some coatings may provide protection against penetrating radiation ("sunscreen"), while others might provide protection against hydration for many hours or even days. Some bio-particles could be coated easily with irrelevant and, therefore, confusing antigenic substances. Thus, although some wet biochemical testing could be expected to help identify certain biological constituents fairly rapidly (for example, as processed by a BIDS[51]), the aerosols may have been so well prepared ("weaponized") that the only near-term conclusion is that a foreign aerosol has been inserted into a specific region that was previously devoid of such content. The aerosol detector networks must be capable of detecting such events, with or without subsequent biochemical analyses and identification. The networks must also be capable of characterizing entirely new aerosol classes relative to any that had been cataloged previously. The anthrax spores sent out in letters were cleverly prepared so as to eliminate any physical features that might produce clumping—by electrostatic charge effects, for example. Compared to conventional untreated bacterial spores, these appear to have had their surfaces specially modified to prevent the buildup of such charges. It would be expected that their surface antigens were quite different from those associated with normal anthrax spores.

Although the National Academies report focused entirely on U.S. capabilities and activities, many other countries maintain active research and development programs in biological and chemical defense. In reviewing the programs of two of the largest—the British and the Canadian—we find that no types of early-detection techniques are being developed other than those already within the scope of the National Academies report. Interestingly, the British Defence Evaluation and Research Agency Porton Down activity,[52] an agency of the Ministry of Defence, solicits customers worldwide to establish partnering relationships in chemical and biological defense. It states, for example, that the U.S. Department of Defense is one of its customers. The U.S. Defense Threat Reduction Agency, which employs over 90 professionals, claims to have "developed the most advanced threat detection capabilities in the world today," yet a perusal of its website and literature offers few clues as to which of these capabilities are different from any discussed in the National Academies report. A similar review of the Canadian Biological Aerosol Facilities at the Defence Research Establishment Suffield[53] confirms that it too is involved in research areas similar to those described in the National Academies report. The Canadian work on "Rapid Detection and Identification of Biological and Chemical Agents by Immunoassay, Gene Probe Assay and Enzyme Inhibition Using a Silicon-Based Biosensor" is similar to the approaches being used in the United States.

The Aerosol Particle Analyzer

One of the simplest (in concept), yet most powerful, means for the rapid *in situ* characterization of individual aerosol particles comprises a localized point-source collection system (shown schematically in Figure 1) that samples its ambient environment by drawing in an airstream in which the aerosol particles are entrained. The sampled aerosol particles (1) are diluted, as required, by an aerosol-handling module (2) to ensure a flow of particles, one at a time, through a fine light beam produced by a laser (3). This laser beam lies along a diameter of a spherical scattering chamber (4) and intersects at the center of the chamber the aerosol stream constrained to pass along another diameter of the chamber. As each aerosol particle passes through the beam, it produces a pulse of light scattered in a spherical wave that is then detected by a plurality of preselected detectors (5). The analyzed particles (6) then exit through an exhaust (7). As each detector lies at a unique angular location (q,f), the measurement is often referred to as a "multiangle light scattering" measurement. Such collection and detection concepts were developed and confirmed many years ago and formed the basis of the so-called aerosol particle analyzer[54] (APA) when combined with computer means containing appropriate analytical software.

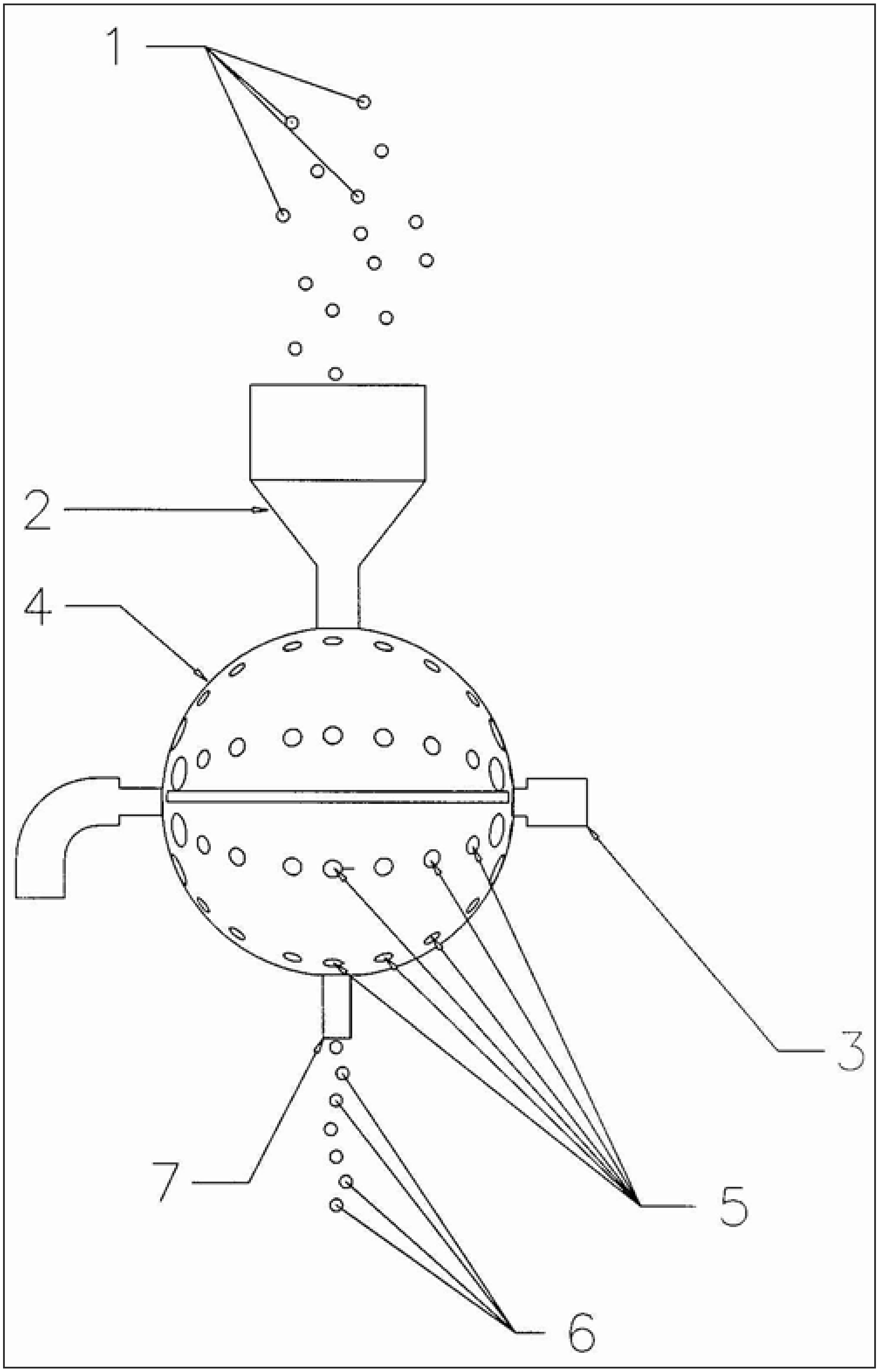


Figure 1. Schematic of key aerosol particle analyzer elements

Figure 2 shows an early version of the APA as implemented for research purposes at the University of Minnesota. The outer diameter of the scattering chamber was about 100 mm, and the argon-ion laser produced about 10^5 W/m^2 at the target aerosol particles passing through the beam. The signals were collected by the optical fibers shown and transmitted to a bank of photomultiplier tubes. Not surprisingly, this was an approach overlooked in the National Academies report. There are at least three reasons for this oversight: The basic objective of the National Academies study was to recommend research and development programs to improve the *medical* response to such attacks. Second, the committee that prepared the report did not have any members who were skilled in or familiar with electro-optical detection techniques. Finally, there is little evidence that the government's research and development efforts in detection technology before about 1990 were searched or considered. The basic makeup of the committee was in keeping with its primary objectives.

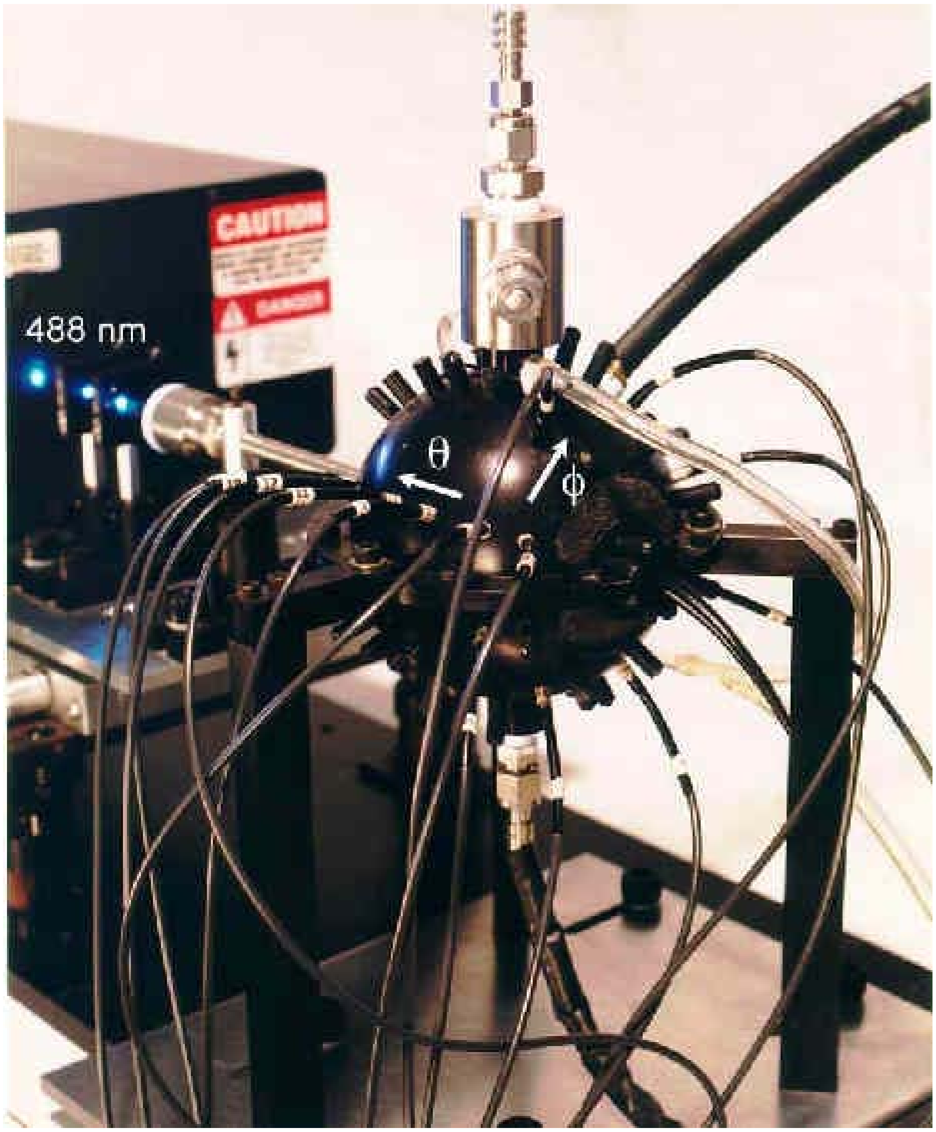


Figure 2. Original research APA, including the associated elements shown: argon-ion laser operating at 488 nm, scattering chamber of 100 mm outer diameter and 40 mm inner diameter, optical fibers that collect and transmit scattered signals to a bank of photomultiplier tube detectors, and aerosol-handling elements.

Of all measurements that may be made in real time on aerosol particles, one at a time, the greatest amount of information available comes from those involving light scattering and its associated implementations. This characterizing information may be further expanded by fitting the individual detectors within an APA detector station with optical analyzers of various types (polarizers, quarter and half wave plates, interference filters, liquid crystal variable retarders, etc.), but by far the most important feature of an APA detector station would be its ability (under suitable software control) to recognize the appearance of aerosol types that may be *different* from those that may have been stored previously for classification purposes. For example, though the optical observables characteristic of anthrax spores might be saved in a reference collection against which those from a newly appearing unknown particle might be compared, the spores themselves (as discussed earlier) might well have been modified before release to confuse such comparisons or to interfere with biochemical tests that might be performed routinely for clinical identification. The spores transmitted via the mails were certainly modified to achieve their special dispersal characteristics. We could expect that such modified spores would produce light-scattering characteristics quite different from any that might have been cataloged previously. Nevertheless, a suitably programmed APA detector station should start enumerating the new particles detected and communicate this information throughout the detector station network to establish a correlation or relationship between the new aerosol and the recently detected aerosol cloud or for the case of letter-delivered puffs.

The basic premise of the multiangle light-scattering technique is that the measurement (using suitable analyzer-fitted detectors), over a sufficient range of both azimuthal and polar angles, of light scattered by an individual aerosol particle contains sufficient information to characterize and classify a wide range of such particles and permit their differentiation by a suitable choice of the so-called optical observable sets selected. The concept was described[55] in 1968 and confirmed in a variety of papers.[56–59] The first instrumentation,[60] developed under Government contract with the U.S. Army Armament, Munitions and Chemical Command, was introduced in 1986 and is still frequently used. It includes means to measure scattered light intensities and polarizations at a plurality of scattering angles from individual aerosol particles. Included among its capabilities was the ability to classify and, thereby, differentiate spores,[61] bacteria,[62] flyash,[63] photochemical smog particles,[64] and similar particle classes. The basis for using these measurements to create a set of optical observables by which means such particles could be differentiated and characterized was described in another paper[65] concerning the explicit identification of various phytoplankton. There are significant further advantages of a deployed interactive network comprising such APA detector stations. Foremost among them is the ability to provide improved levels of aerosol characterization and *all* of the operating capabilities summarized following Table 1. The multiplicity of independent measurements of the aerosol threat at different physical locations and times can be used further to refine presumptive particle characterizations. For example, toxins deployed as aerosolized droplets may well exhibit evaporation effects that will result in a changing particle size distribution, easily detected and monitored by individual stations of the APA detector station network components. Indeed, a great number of liquid droplet-deployed chemical agents may be detected readily and characterized by the same instrumentation used to characterize bio-aerosol clouds.

Continuing research efforts have been in progress for many years to explore and develop point-source detectors incorporating light-scattering measurements. The U.S. Army Applied Research Laboratories have expanded their own intramural facilities significantly while supporting important contract research with leading technical groups throughout the United States and abroad.[66] For example, as discussed earlier, fluorescence spectrum analyzers for the measurement of single bio-aerosol particles are being explored as a characterization technique for such particles.[67] During the period since the first APA was delivered,[68] there have been numerous developments that could accelerate the deployment of APA-based detector stations. Solid-state laser sources operating at high power efficiency have become readily available together with compact high-sensitivity detectors. Integrated digital signal-processing chips are far more powerful, compact, and inexpensive than they were just a few years ago. Such chips preprocess the signals from each detector within the APA. Wireless technology has evolved so rapidly that complete communications devices, including power supplies, are available in formats not much larger than a wristwatch. Fabrication costs have fallen as performance has accelerated.

Consider a system capable of classifying and processing about 50,000 aerosol particles per minute. Such processing would include all associated data reduction and telecommunications with the central station required to associate a given measurement with a particular class of threat. (Classification would include the so-called "unusual" designation.) Were some particles evaporating or hydrating over time, these properties could be discernable as well if a sufficient population were present within a reasonable period (for example, several minutes) of analysis. If the laminar sheath entrained aerosol stream moved at a rate of 2 m/sec through a laser beam of 0.5 mm diameter, the time for passage of a single particle through this beam would be about <\/nobr>250 µseconds. The volume of aerosol examined per minute would be about 500 µl. This would correspond to a maximum sampled density of 10^5/ml, well above the level of the anthrax spore swath discussed earlier. Even under the most extreme particle loading, the APA devices could easily process the samples presented.

One of the most interesting and desirable elements of the multiangle light-scattering measurement technique employed by an APA detector is the ability to examine some important physical properties of each particle passing through its laser beam, no matter what the overall concentration of the particle species may be. Using a 50-mW laser source operating at a wavelength of 690 nm, each particle the size of an anthrax spore would scatter on the order of 10^8 photons during its passage through the laser beam. This is a large number of photons with scattering properties that may be used to classify such particles often in terms of size, shape, refractive index, and anisotropic structure. Such scattering characteristics may be compared against cataloged sets or distinguished from such prior collections based on subtle scattering differences. The important feature to emphasize here is that the characterization of any particle, no matter what its relative population may be, is independent of the properties measured of other members of the targeted set. The early detected threat particles, measured at higher concentrations, would be used by the network to establish optical observables or "fingerprints" for use by detectors more distant from the location of threat insertion or for later measurements once the particle concentrations have decreased.

System Sizes and Costs

The anticipated costs of an updated APA detector station capable of classifying 10,000 to 50,000 particles per minute should be quite reasonable while providing durability unavailable in the past. It is estimated that in quantities of 1,000 units (including programmable aerosol-handling capabilities, telecommunications links, and central stations), the average cost per unit would be $10,000 to $15,000. Once quantities exceed 100,000 units, unit costs should fall to $1,000 or less.

The number of detector stations needed to protect (that is, provide early warning to) a city may be estimated as follows. Neglecting impediments of structures to the intrusion of the threat cloud particles, we would hope for threat detection at station locations that lie no further than 100 m from any intruding elements. The resolution in altitude must be considerably finer than 100 m, as the cloud's interaction with the majority of the targeted population should occur within a very narrow height above the ground (see Table 1, items 9 and 10). This 100-m detector station resolution should be available at, say, the specific elevations of 2, 5, and 10 m. In addition, a detector station at 50 m or the highest position available for that location would provide an additional monitor for clouds/threats delivered at higher, though less effective, altitudes. On this basis, we find a requirement of about 60,081 x 4 ˜ 325 detector stations/km^2. In regions with a large fraction of the ground area occupied by inaccessible structures, this figure could be smaller. Were such structures large occupied buildings (for example, in Manhattan), they might require *additional* customized distributions of detector stations within each building provided, perhaps, by the building ownership itself. These might include stations at air intake locations and other areas readily accessible to outside air as well as individual rooms where, for example, mail and packages are processed for subsequent distribution. Some localized regions containing transient populations (for example, subway stations, stadiums, public meeting areas, and sports arenas) may require specially configured detector station networks. Wider distributed regions comprising single-family homes of one or two stories, such as the greater Los Angeles area, may not require so high a density of detector stations. Peripheral regions through which threat clouds might be successfully launched require additional stations, some of which may be at a greater altitude than assumed above. Special configurations may also be required for critical buildings such as embassies, police stations, and military command centers. With the successful use of mail transmission into congressional buildings, monitors may be needed in offices of congressional staffs and elected officials. Table 2 presents a selection of U.S. cities, their incorporated areas, and the relatively crude estimates of detector stations required to provide such areas with early warning of an intruding aerosol cloud. These figures will need adjustment for the variations of protection associated with specific local factors as discussed above.

Table 2. Estimated detector station requirements for selected cities

City	**Area** (km^2)	**Detector Stations**
Chicago	591	192,000
Dallas	979	318,000
Denver	400	130,000
Los Angeles	1,211	394,000
Manhattan Island	57	19,000
Palo Alto	67	22,000
San Francisco	119	39,000
Santa Barbara	55	39,000
Seattle	375	122,000
Washington, DC	179	58,000

Although the networked APA detector stations alone will provide an almost immediate warning of an intruding aerosol cloud of unknown origin, at minimal incremental cost a simple pulsed ultraviolet source may be added to selected stations to interrogate each analyzed particle for fluorescence—a characteristic often associated with proteinaceous materials. As different types of auxiliary detection measurement techniques become available, they too, may be integrated into selected detector stations. Again it must be emphasized that aerosol particles may be “disguised” easily (weaponized) so as to render many types of expected characteristics, including fluorescence, undetectable.

Remediation: Other Uses of APA Detector Stations

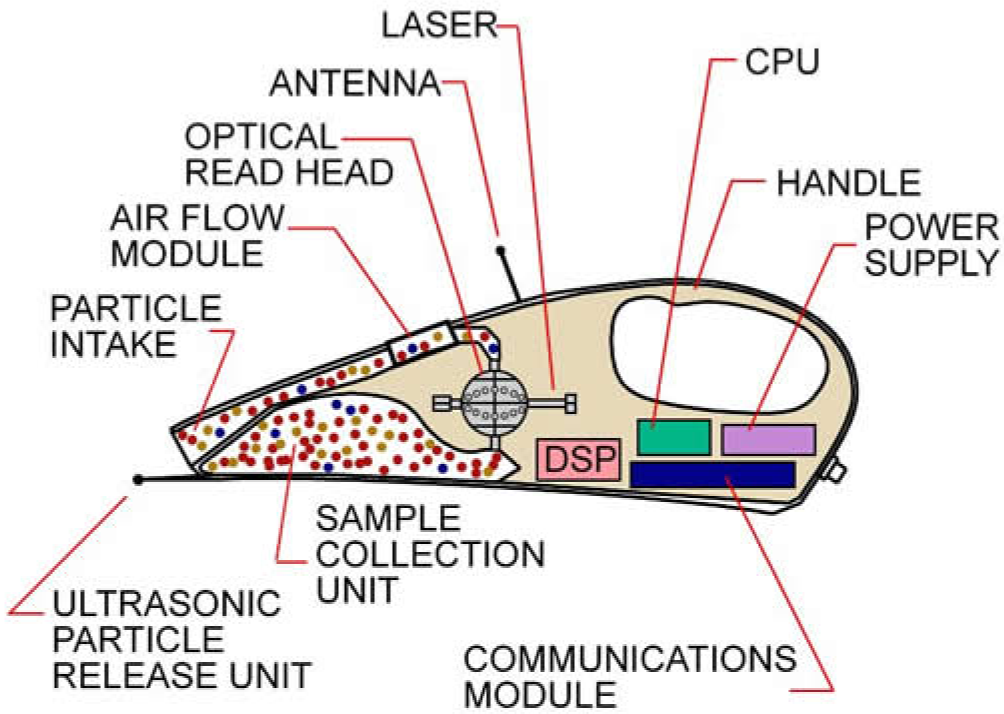


Figure 3. Schematic layout of portable remediation device based on aerosol detection station, including the following elements: APA chamber, programmable central processing unit and associated electronics, ultrasonic particle release mechanism, communications module, and aerosol-handling and collection elements.

Although this article has focused primarily upon the use and importance of early-warning systems, the deployment of anthrax spores throughout the U.S. postal system, federal and congressional office buildings, and private offices has exposed another significant problem of great importance. This concerns the detection and identification of contaminated areas and their remediation. Once a portable APA station has been programmed to recognize the specific optical observables characterizing the biohazard being sought (most recently anthrax spores), it becomes a simple matter to examine various locations that might harbor such agents. The location would be queried by means of an ultrasonic loosening of possible contaminants adhering to surfaces or by use of air bursts (vacuum safety backup capabilities should be available during such activities). A portable, handheld version of an APA would sample the local air regions that had been disrupted. As the targeted particles were identified, the programmed alarm-and-warning system would be activated.

Similarly, the same APA device could monitor the cleanup of specific contaminated regions. Figure 3 shows a schematic view of a proposed portable APA-based device.

Conclusions

So where does the threat of a bioterrorist attack stand? The threat is certainly serious and, whether exaggerated or not, has had some significant consequences already. The relative ease by which deliveries of anthrax spore puffs into offices and postal sorting stations have been achieved suggests that, targeting local, relatively small segments of the population, the problem is becoming far more serious. The accelerating support for related research and development mandated by Congress has resulted in a virtual bonanza for many programs that have even a remote relationship to the subject. Some of these programs are wasteful of the funds expended on them, as they duplicate similar efforts supported by the Defense Department many decades earlier. Others, especially in areas related to the rapid diagnosis of infectious diseases, are of great immediate benefit and will contribute significantly to improved health care for many of the world's populations most vulnerable to the diseases targeted by the new diagnoses. Without the current feelings about the threat of bioterrorism, these programs probably would have had a minimal chance for governmental support. In addition, the need to establish a coordinated response between diverse governmental agencies and health care providers in the event of any such catastrophe is being given well-deserved additional attention and funding through support by the federal government. Recent experiences, however, suggest that such coordination has a long way to go.

One of the most impressive confirmations of the need for an early-warning network was the demonstration, by means of a simulated attack, that without such warning the results would be catastrophic. In 1999, Congress directed the Department of Justice to conduct an exercise engaging key personnel in the management of mock chemical, biological, or cyberterrorist attacks. The resulting exercise was called "Topoff," named for its engagement of top officials of the U.S. government. The mock bioterrorist attack was located in Denver and began on 20 May 2000. The major conclusion of the exercise was summarized in an article by Thomas V. Inglesby et al.[69] "The systems and resources now in place would be hard-pressed to successfully manage a bioweapons attack like that simulated in TOPOFF." Amy Smithson of the Henry L. Stimson Center, a group that promotes international strengthening[70, 71] of and compliance with the Biological and Toxin Weapons Convention of 1972, was far more critical in her statement before Congress:[72] "This exercise … graphically demonstrated the shortcomings of the federal government's organizational structure.… the road to Hades is paved with decisions by committee." Her predictions were borne out by the lack of a coordinated response to the events surrounding the letter attacks then in progress. Indeed, despite the Government support for early detection of bioterrorist threats, neither the Army Research Laboratories Chemical and Biological Aerosols Team website nor the Stimson Center's report *House of Cards* mentioned how early warning or detection might have significantly changed the course of the simulated attack. None of the tools (for example, BIDS) purportedly developed by the government specifically to speed up the detection of an in-progress attack was mentioned in any of the reports of the exercise.

Early warning will continue to represent the best defense against a successful bioterrorist attack. However, the successful delivery of an aerosol cloud is not as easily achieved as proposed. Even before their infamous attack on the Tokyo subway system, the Aum Shinrikyo cult[73] had tried repeatedly without success to use biological agents for attacks on local populations. The delivery of such a threat at the proper altitude and under suitable atmospheric conditions to a major urban population center is an extremely difficult task requiring far greater sophistication than is commonly believed. Proposed releases from aircraft, trucks, or other vehicles would be detected by appropriately distributed detector stations almost immediately after deployment and long before the aerosol reached significant targets. Immediate detection in closed rooms or areas under directed attack via the mails could have prevented many of the injuries and deaths reported to date. As mentioned earlier, typical inhalable aerosols fall so slowly that their introduction by aircraft means seems unlikely, though crop dusters apparently have received some attention recently. Attacks by missile means, such as purportedly planned by the Iraqis[74] during and following the Gulf War, can deliver quickly and at the correct altitude biological agents to military targets. However, the appearance of the missile itself or a crop duster, were such used, is as early a warning as possible, though the detector stations present would still provide a rapid confirmation of the aerosol's presumptive composition and danger, as well as the dynamics of its distribution throughout the targeted region. The delivery of specially prepared anthrax spores via the mails has proven remarkably simple and effective though by no means a technique of mass destruction. The preparation of the spores, however, appears to have required an extraordinary amount of skill found only in a few laboratories throughout the world.[75]

There are three distinct elements that suggest, therefore, that the threat of a bioterrorist attack may be diminished soon. First, as discussed, is the fact that massive aerosol cloud-based attacks are extremely difficult to implement. Second is the hope, though perhaps unlikely, that the historical aerosol of choice comprising *B. anthracis* spores may no longer be attractive because of the possibility of a universal antitoxin effective irrespective of the engineered antibiotic susceptibility of the anthrax organism.[76] Before such a hope may be realized, however, a great amount of research and study will be required to address the potential problems associated with the use of mutant protective antigen as discussed earlier. Finally, technology exists that can provide extensive point-source detection networks, with their concomitant ability to provide real-time warning of an attack in progress. With such a warning, the casualties within virtually any civilian target might well be reduced significantly.

Despite the numerous strategies proposed to cope with the consequences of a successful biological attack, there can be no greater urgency than the immediate and continuing deployment and refinement of point-source APA detector stations and their associated networks throughout the numerous vulnerable sites. This is a long and expensive task, but each unit deployed will represent a further diminution of the dangers associated with biological and, in many cases, chemical terrorism. In this latter regard, the National Academies report states, "Terrorist incidents involving biological agents, especially infectious agents, are likely to be very different from those involving chemical agents, and thus demand very different preparation and response." The use of the mails for delivery of attacks using anthrax spores confirms this conclusion. However, the APA stations proposed may detect those chemical incidents that involve aerosolized delivery mechanisms, and, in this case, the National Academies conclusion might require some revision. Most important, such proposed networks do not serve only an antiterrorist purpose; they concomitantly provide the means by which the natural environment may be monitored for other dangerous aerosol particulates, both man-made and natural. The correlation between inhaled particulate matter (such as carbon particles) and cancer has been known for many years. New federal regulations have been proposed to control and prevent hazardous particulate releases into the atmosphere and workplace. Not only will regulations governing the workplace be expanded to include each class of aerosol particle subsequently found to pose a health hazard; much of the environment throughout populated regions will fall under further scrutiny as the effects of particulates on human health are better understood. The concept of a distributed network of collaborative point-source APA detectors will prove equally useful in detecting and providing early-warning alarms of potentially hazardous particles such as soot, smog, asbestos fibers, and accidental toxic aerosol releases from industrial sources. Thus the deployment of extensive APA-based detector networks, while providing early warning of many classes of bioterrorist (and some chemical terrorist) attacks in progress, will provide immediate and continuing localized aerosol-monitoring capabilities. The multipurpose utility of deployed APA networks permits their application immediately to efforts intended to improve the local environment while providing some comfort to the local populations they are intended to protect against a variety of possible terrorist threats. The conditioning and preparation of the local populations so protected for the appearance of environmentally dangerous aerosols and the subsequent alarms provided by the monitoring stations will play a major role in diminishing the psychological panic associated with a purely terrorist attack.

Acknowledgements

The suggestions, clarifications, and education provided to the author by Professor Matthew Meselson were invaluable during the many revisions of this paper. The early encouragement and comments by Professor Edward Adelberg were equally useful in bringing together many of the microbiological details and ideas. The comments and observations of Dr. Peter Rosen were also important, as were the more physics-specific remarks of my colleagues Dr. Steven Trainoff and Dr. Miles Weida.

References

Click on an end note number to return to the article.

1. *NATO Handbook on the Medical Aspects of NBC Defensive Operations, Part II—Biological* (Washington, DC: Departments of the Army, Navy, and Air Force), 1 February 1996.

2. Cf. Norman F. Cantor, *In the Wake of the Plague: The Black Death and the World It Made* (New York: The Free Press, 2001).

3. C. Gregory Smith, "Bioterrorism," *North Carolina Medical Journal*, Vol. 61, 2000, pp. 150–165.

4. Cf. *Emerging Infectious Diseases*, Vol. 5, No. 4, July–Aug. 1999.

5. Barry Kellman, "Biological Terrorism: Legal Measures for Preventing Catastrophe," *Harvard Journal of Law & Public Policy*, Vol. 24, 2001, pp. 417–488.

6. Ibid.

7. *Chemical and Biological Terrorism: Research and Development to Improve Civilian Medical Response* (Washington, DC: National Academy Press, 1999); http://www.nap.edu/books/0309061954/html/index.html.

8. *NATO Handbook on the Medical Aspects of NBC Defensive Operations, Part II—Biological*.

9. *Chemical and Biological Terrorism*.

10. Carina Dennis, "The Bugs of War," *Nature*, Vol. 411, May 2001, pp. 232–235.

11. *Chemical and Biological Terrorism*.

12. NATO Handbook on the Medical Aspects of NBC Defensive Operations, Part II—Biological.

13. Ibid.

14. *Chemical and Biological Terrorism*.

15. Bret R. Sellman, Michael Mourez, and R. John Collier, "Dominant-Negative Mutants of a Toxin Subunit: An Approach to Therapy of Anthrax," *Science*, Vol. 292, 27 April 2001, pp. 695–697.

16. Cf. Jonathan B. Tucker, "Historical Trends Related to Bioterrorism: An Empirical Analysis," Emerging Infectious Diseases, Vol. 5, No. 4, July–Aug. 1999, pp. 498-504.

17. First National Symposium on Medical and Public Health Response to Bioterrorism, Arlington, VA, February 1999; Second National Symposium on Medical and Public Health Response to Bioterrorism, Washington, DC, November 2000; Unified Science & Technology for Biological Threat Reduction, Albuquerque, NM, March 2001.

18. Johns Hopkins University, Schools of Public Health and Medicine, Center for Civilian Biodefense Studies, Baltimore, MD; the Southern Research Institute Chemical and Biological Defense Division, Birmingham, AL; University of New Mexico Center for Advanced Studies, Albuquerque.

19. See the extensive bibliographies in C. Gregory Smith, "Bioterrorism"; Jonathan B. Tucker, "Historical Trends Related to Bioterrorism: An Empirical Analysis"; Barry Kellman, "Biological Terrorism: Legal Measures for Preventing Catastrophe"; and *Chemical and Biological Terrorism*.

20. *Chemical and Biological Terrorism*.

21. David R. Walt and David R. Franz, "Biological Warfare Detection," *Analytical Chemistry*, Vol. 72, 1 Dec. 2000, pp. 738A–746A.

22. *Chemical and Biological Terrorism*.

23. Ibid.

24. Elinor Langer, "Chemical and Biological Warfare (I): The Research Program," *Science*, Vol. 155, 13 Jan. 1967, pp. 174–179.

25. Elinor Langer, "Chemical and Biological Warfare (II): The Weapons and the Politics," *Science*, Vol. 155, 1967, pp. 299–303.

26. Elinor Langer, “Chemical and Biological Warfare (I): The Research Program.”

27. Ibid.

28. C. Gregory Smith, “Bioterrorism.”

29. Barry Kellman, “Biological Terrorism.”

30. *Chemical and Biological Terrorism*.

31. *Effects of Biological Warfare Agents* (Washington, DC: Department of Health, Education, and Welfare, July 1959).

32. H.R. 525, introduced by Wayne Gilchrest.

33. *Chemical and Biological Terrorism*.

34. A. Bovallius, B. Bucht, R. Roffey, and P. Anas, “Three-Year Investigation of the Natural Airborne Bacterial Flora at Four Localities in Sweden,” *Applied and Environmental Microbiology*, Vol. 35, 1978, pp. 847–852; W. M. Li, S. C. Lee, and L. Y. Chan, “Indoor Air Quality at Nine Shopping Malls in Hong Kong,” *Science of the Total Environment*, Vol. 273, 2001, pp. 27-40.

35. *Emerging Infectious Diseases*, Vol. 5, No. 4, July–Aug. 1999.

36. Matthew Meselson, Jeanne Guillemin, Martin Hugh-Jones, Alexander Langmuir, Ilona Popova, Alexis Shelokov, and Olga Yampolskaya, “The Sverdlovsk Anthrax Outbreak of 1979,” *Science*, Vol. 266, 1994, pp. 1202–1208.

37. Manabu Shimada, Kikuo Okuyama, Yasljo Kousaka, and Daiki Minamino, “Experimental Study of Aerosol Deposition in Stirred Flow Fields Ranging From Laminar to Turbulent Flows,” *Journal of Chemical Engineering of Japan*, Vol. 24, 1991, pp. 203–209.

38. A. Stohl, M. Hittenberger, and G. Wotawa, “Validation of the Lagrangian Particle Dispersion Model Flexpart Against Large Scale Tracer Experiments,” *Atmospheric Environment*, Vol. 24, 1998, pp. 4245-4264.

39. David R. Walt and David R. Franz, “Biological Warfare Detection.”

40. Cf. P. P. Hairston and F. R. Quant, “System for detecting fluorescing components in aerosols,” U.S. Pat. No. 5,999,250 (1999).

41. B. L. Ulrich, D. Smith, and R. N. Keeler, “Spectrally dispersive imaging lidar system,” U.S. Pat. No. 5,257,085 (1991).

42. *Chemical and Biological Terrorism*.

43. David R. Walt and David R. Franz, “Biological Warfare Detection.”

44. David W. Siegrist, “The Threat of Biological Attack: Why Concern Now?” *Emerging Infectious Diseases*, Vol. 5, No. 4, July–Aug. 1999, pp. 505–512.

45. Matthew Meselson, Jeanne Guillemin, Martin Hugh-Jones, Alexander Langmuir, Ilona Popova, Alexis Shelokov, and Olga Yampolskaya, “The Sverdlovsk Anthrax Outbreak of 1979.”

46. Ibid.

47. O. G. Raabe, Chap. 2 in *Mechanisms of Respiratory Toxicology*, H. Witschi and P. Nettesheim, eds. (Boca Raton, FL: CRC Press, 1982).

48. Cf. E. Murad and C. P. Pike, U.S. Pat. No. 5,898,373, “Method for monitoring a site for the future presence of toxic agents,” April 1999.

49. Ronald G. Pinnick, Steven C. Hill, Paul Nachman, Gorden Videen, Gang Chen, and Richard K. Chang, “Aerosol Fluorescence Spectrum Analyzer for Rapid Measurement of Single Micrometer-Sized Aorborne Biological Particles,” *Aerosol Science and Technology*, Vol. 28, Issue 2, February 1998, p. 95.

50. *Chemical and Biological Terrorism*.

51. David R. Walt and David R. Franz, “Biological Warfare Detection.”

52. See www.dera.gov.uk for an overview of these activities in the UK.

53. See dres.dnd.ca for an overview of these activities in Canada.

54. Philip J. Wyatt, Kevin L. Schehrer, Steven D. Phillips, Christian Jackson, Yu-Jain Chang, Randall G. Parker, David T. Phillips, and Jerold R. Bottinger, “Aerosol Particle Analyzer,” *Applied Optics*, Vol. 27, Issue 2, Jan. 1988, p. 217.

55. Philip J. Wyatt, “Differential Light Scattering: A Physical Method for Identifying Living Bacterial Cells,” *Applied Optics*, Vol. 7, Issue 10, October 1968, p. 1879.

56. Philip J. Wyatt, “Identification of Bacteria by Differential Light Scattering,” *Nature*, Vol. 221, 1969, p. 1257.

57. Philip J. Wyatt, “Light Scattering in the Microbial World,” *Journal of Colloid and Interface Science*, Vol. 39, 1972, p. 479.

58. D. T. Phillips, R. M. Berkman, and P. J. Wyatt, “Measurement of the Lorenz-Mie Scattering of a Single Particle: Polystyrene Latex,” *Journal of Colloid and Interface Science*, Vol. 34, 1970, p. 159.

59. Philip J. Wyatt, “Cell Wall Thickness, Size Distribution, Refractive Index Ratio, and Dry Weight Content of Living Bacteria (*Staphylococcus aureus*),” *Nature*, Vol. 226, 1970, p. 277.

60. Philip J. Wyatt et al., “Aerosol Particle Analyzer.”

61. Philip J. Wyatt, “Observations on the Structure of Spores,” *Journal of Applied Bacteriology*, Vol. 37, 1975, p. 48.

62. Philip J. Wyatt and D. T. Phillips, “Structure of Single Bacteria From Light Scattering,” *Journal of Theoretical Biology*, Vol. 37, 1972, p. 493.

63. Philip J. Wyatt, “Some Chemical, Physical and Optical Properties of Fly Ash Particles,” *Applied Optics*, Vol. 19, Issue 6, March 1980, p. 975.

64. D. T. Phillips and Philip J. Wyatt, “Single-Particle Light-Scattering Measurement: Photochemical Aerosols and Atmospheric Particulates,” *Applied Optics*, Vol. 11, No. 9, Sept. 1972, p. 2082.

65. Philip J. Wyatt and C. Jackson, “Discrimination of Phytoplankton Via Light-Scattering Properties,” *Limnology and Oceanography*, Vol. 34(I), 1989, p. 96.

66. Army Research Laboratories (U.S. Army Materiel Command) Chemical and Biological Aerosols Team organization and activities.

67. Ronald G. Pinnick, Steven C. Hill, Paul Nachman, Gorden Videen, Gang Chen, and Richard K. Chang, “Aerosol Fluorescence Spectrum Analyzer for Rapid Measurement of Single Micrometer-Sized Aorborne Biological Particles.”

68. Philip J. Wyatt et al., “Aerosol Particle Analyzer.”

69. Thomas V. Inglesby, Rita Grossman, and Tara O’Toole, “A Plague on Your City: Observations From Topoff,” *Clinical Infectious Diseases*, Vol. 32, 2001, pp. 436–445; http://www.journals.uchicago.edu/CID/journal/issues/v32n3/001347/001347.html.

70. Amy Smithson and Leslie-Anne Levy, *Ataxia: The Chemical and Biological Terrorism Threat and the US Response* (Washington, DC: Henry L. Stimson Center, Report 35, Oct. 2000); http://www.stimson.org/cbw/pubs.cfm?id=12.

71. *House of Cards: The Pivotal Importance of a Technically Sound BWC* [Biological Weapons Convention] *Monitoring Protocol* (Washington, DC: Henry L. Stimson Center, Report 37, May 2001); http://www.stimson.org/cbw/pubs.cfm?ID=13.

72. Amy Smithson, prepared statement before the House Committee on Government Reform, Subcommittee on National Security, Veterans Affairs, and International Relations, and the House Committee on Transportation and Infrastructure, Subcommittee on Economic Development, Public Buildings, and Emergency Management (24 April 2001); http://www.house.gov/transportation/pbed/04-24-01/smithson.html.

73. Amy Smithson and Leslie-Anne Levy, *Ataxia*.

74. Christopher J. Davis, "Nuclear Blindness: An Overview of the Biological Weapons Programs of the Former Soviet Union and Iraq," *Emerging Infectious Diseases*, Vol. 5, No. 4, July-Aug. 1999, pp. 509–512; http://www.cdc.gov/ncidod/eid/vol5no4/pdf/v5n4.pdf.

75. Cf. *New York Times*, 24–25 October 2001, various stories.

76. Bret R. Sellman, Michael Mourez, R. John Collier, "Dominant-Negative Mutants of a Toxin Subunit."