

John Bartlett and Bioterrorism

The possibility that microbes might be deployed as biological weapons is a frightening prospect. It was sufficiently alarming that in 1972, the nations of the world signed a convention pledging to destroy all biological weapons and to cease all offensive research programs utilizing them (1). For 20 years, there was a complacent belief that all had complied but then serious concerns arose. Important actions were needed to prepare the country to at least deal with the major threat agents of smallpox and anthrax. But how to galvanize the will was not clear. John was deeply concerned and, with others, took initiatives to deal with the challenge. I was asked to speak with you regarding bioterrorism, of John's role in this field, as well as the future. Some historical perspective is necessary to appreciate the importance of the problem and the unusual role it occupied in the infectious disease field.

A key event in the evolution of this story was a Symposium at the Infectious Diseases Society of America (IDSA) opening meeting on September 13, 1997. It awakened a key group to the menace posed by microbes as weapons—indeed, of their potential to rewrite human history. At that time, the challenge of emerging infections, such as AIDS and Ebola Virus were a growing concern. John Bartlett was the Society president that year but personally as much concerned about the threats posed by biological weapons. They were, after all, a category of emerging threats—threats for which we were ill-prepared. However, the topic of bioterrorism had not previously been discussed at a professional meeting such as this. In fact, it had been little discussed at all, even in schools of medicine and public health. Beginning in September, 1997, that changed.

As a matter of history, it is important to recall that a half century ago, Nobel Laureate Macfarlane Burnett as well as prominent leaders in medicine in this country announced that the infectious diseases had effectively been conquered—that the time had come for medical expertise and resources to shift their primary attention to the chronic diseases. At that time,

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John and I were barely embarked on our careers in the infectious disease field. Not an encouraging pronouncement but, for us, it was too late. We were committed!

Indeed, the dimensions of the infectious disease field did change. Vaccines, antibiotics, and broad advances in care minimized the impact of the infectious diseases. During a period extending over some 20 years, infectious disease residencies decreased in number and microbiology departments diminished in size or merged. In 1972, all nations signed the 1972 biological weapons convention, thus providing even more confidence that there were no hidden threats about which to be concerned.

In 1984, AIDS provided a rude jolt to modern medicine's confidence in being able to handle major, unexpected challenges. The problem grew steadily worse before some rays of hope for treatment and prevention appeared. Progress was slow but one of the few beacons of sanity and hope was Hopkins with needed critical leadership being provided by John Bartlett.

Bioweapons become of greater concern

In the medical community --indeed, throughout the country --biological weapons were spoken of as being "morally repugnant" and not a subject for open discussion, instruction, or research. But, in late 1992, Soviet defector, Ken Alibek, Deputy Director of the Soviet Union's BW program brought news of large, sophisticated laboratories in the USSR, working with botulism, smallpox, anthrax, and plague as well as recombinants involving Ebola and Venezuelan encephalitis viruses (2). The information was regarded with disbelief. In the U.S. there were very few laboratories that had any expertise in dealing with the principle agents of greatest concern -- anthrax, plague, or smallpox.

In 1995, an especially disturbing event occurred. A Japanese religious cult, Aum Shinrikyo, released lethal amounts of sarin in the Tokyo subway system. It was later learned that they also sprayed large quantities of anthrax organisms throughout Tokyo on several occasions but the non-virulent vaccine strain they mistakenly used caused no deaths (3).

Coping with New Challenges

In July 1995, heightened concern about terrorism resulted in President Clinton issuing a special Presidential Decision Directive (3). It stipulated that

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measures for planning and implementing counterterrorism programs be undertaken. The Departments of Defense, Justice, and Energy were given \$53 million to help establish "first responder" teams in 120 cities and to train and equip mobile military response units. No funds were given to HHS. The responder teams comprised police, fire, and emergency rescue staff. Much of the training was conducted at the Army's Chemical Weapons facility and dealt primarily with explosive devices and chemical weapons. Little was said about biological weapons or early detection and management of outbreaks, or about the care and management of casualties. At that time, neither CDC nor NIH had personnel or expertise in dealing with biological weapons (4).

It was inconceivable to John and I that health resources could be entirely overlooked. Medicine and public health with community resources would have to play the major role in dealing with a BW attack. We believed the existing policies should be more widely known and government leadership persuaded of the need for support to deal with medical issues..

John Bartlett was an enthusiast and ideal leader with his positions as head of infectious diseases at Johns Hopkins and as President of the IDSA; Mike Osterholm was an excellent public health complement as he was then Past President of the Council of State and Territorial Epidemiologists. I brought 6 years of experience at the White House and HHS.

The national IDSA meeting was an ideal opportunity to educate colleagues about biological weapons as well as emerging infections. It was fortunate that a recently published, best-selling book, the "Hot Zone", dealt with the threat of new microbial agents (5). It detailed a dramatic escape of the hemorrhagic Ebola virus from a laboratory in Reston Virginia. Its author, Richard Preston was an enthusiastic speaker, personally concerned, and anxious to participate. The only available space was an exceptionally large auditorium, far bigger than we needed but, on the afternoon of September 13, the audience streamed into the auditorium in unbelievable numbers. Publicity about the Soviet program and the Japanese attack were partially responsible; Richard Preston was an attraction; John Bartlett's advocacy was a factor. It

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resulted in a standing room only audience – an estimated 2500. It included many physicians who could imagine they themselves being on call to emergency rooms to see patients with strange, severe diseases.

In discussing the urgent needs for a wider appreciation of the threat, two hypothetical challenges were posed. What might be the diagnosis and response for a desperately ill patient with high fever who was thought to have pneumonia, had difficulty breathing and appeared to be close to terminal. A chest x-ray provided no clue. As he was being examined, two other patients with severe pneumonia were brought into the emergency room from a nearby area. Early treatment was urgent. Could the cases be related? What might they have? Would anyone consider anthrax? Another case: a 15 year-old boy who was desperately ill with three days of a very high fever and had small vesiculo-pustular lesions over his face and lower arms. He had been successfully vaccinated against measles and was consuming no drugs of any sort. How many might think of smallpox as a possibility? After all, there hadn't been a case anywhere in the world for 30 years.

I posed the question to the audience: "What would you do as the on-call infectious disease consultant at 8:00 PM on a Saturday night?"

From a Symposium to Action to a Center The symposium began to stimulate considerable interest among physicians and the public. Soon, John and I were presenting at hospital grand rounds, scientific group meetings, and to lay groups. Media interviews were plentiful. Many encouraged us to establish a Center in order to increase the number of personnel and extend the educational effort. Senior leadership at 10 likely foundations was approached. Each expressed personal interest and concern. However, they quite frankly stated that their Boards would not want to be identified with activities, however well-meaning, that dealt with "morally repugnant" instruments of war. Schools of Medicine and Public Health were of a like mind and many used the term "morally repugnant".

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Our first programmatic initiative evolved unexpectedly when I was invited as an observer in a New York City day-long "table top exercise" in which Mayor Rudy Giuliani would be an active participant. Other observers included representatives from a number of government agencies. A contractor presented an anthrax attack scenario and led a discussion about steps to be taken. I was startled by the number of misperceptions and the number of erroneous assertions. One conclusion that the group was led to accept was that southern Manhattan would have to be quarantined and disinfected – a technically impossible and wholly unnecessary feat. Something had to be done to provide informed guidance. All agreed but this was seen to be problematic given the number of agencies involved. They strongly urged that we at Johns Hopkins convene an informal invitation-only working group at Johns Hopkins.

This we did. We invited some 25 persons representing relevant government agencies plus state and local health department staff, and academia. Despite only 2 weeks advance notice of the several meetings we convened, attendance was consistently more than 90%. As a first step, we reviewed a list of more than 30 possible organisms that could be utilized as possible biological weapons. In discussion, priorities were identified based on characteristics of the organisms and feasibility of preparedness and response strategies. Six organisms were selected as being of highest priority. These are now referred to as the Class A agents (3).

There was a further problem as there were no ready references at that time that provided readable but concise medical and public health information about the six diseases or actions that should be taken. Accordingly, expert subgroups drafted disease-specific chapters. These were reviewed by the entire group and published in JAMA. References for two of the six are shown (6)(7). The Journal's weekly distribution of more than 300,000 copies assured wide dissemination.

The Center Comes into Being In May 1998, at the President's request, the Congress approved \$175 million for the FY99 budget in support of an HHS budget. Senator Mikulski pledged her support for a Hopkins Center and earmarked one million dollars in the budget. With

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resources in view, the Center for Civilian Biodefense Studies was established in September 1998. John and I served as Joint Directors. There were three other professional staff: Drs. Tara O'Toole, Tom Inglesby, and Monica Schoch-Spana. Not many months later, the Alfred P. Sloan Foundation expressed its confidence in the Center with a multi-million dollar grant and continuing encouragement which extended for more than a decade.

A primary goal for the Center was to foster an understanding of the need for the establishment of community-wide planning to deal cohesively with medical and public health preparedness and response. This implied the need for developing knowledge and skills among a diverse array of professional and public participants. Thus, in February 1999, we sponsored the First National Symposium on Medical and Public Health Response. We had an over flow registration for a 1000 seat auditorium in Washington. A second symposium one year later was received with comparable enthusiasm. Thus, in just 24 months, we were well under way in establishing the fact that medicine and public health, hospitals, and community organizations were critical to the entire threat agenda. Encouraged, we established a website and started a newsletter which was the precursor of the journal, *Bioterrorism and Biodefense*, now in its 10th year and a premier publication in its field.

Dark Winter –a unique exercise only weeks before September 11, 2001 Educating and persuading professional colleagues of the vital importance of a program is a challenge; persuading Congress and the President is a more daunting task. In 2001, we decided to develop an exercise to simulate the events which could be expected following the release of smallpox in an American city (8). The critical issues that immediately would arise and the adequacy of the national emergency response capability would be reflected in the perceptions and actions of simulated meetings of the National Security Council. Twelve senior officials, including former Cabinet-level officials assumed roles as National Security Council members. In

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the role of President, former Senator Sam Nunn, chaired the deliberations. Correspondents from three television networks and two newspapers attended and publicized the exercise.

A smallpox attack was chosen for the scenario because of its severity, its capability to spread, and the problems of how to distribute 15 million doses of vaccine in a population of 280 million. Participants discussed the options and actions to be taken immediately following discovery and at 2 and 4 weeks afterwards as the disease spread.

The exercise vividly illustrated the complex array of problems in coordinating government actions to mobilize personnel, vaccines, and health facilities to care for patients, to confirm cases, to mount vaccination efforts. Communications with officials throughout the country would be necessary as well as with the public. But what were the messages, who should be delivering them, and through what media? Questions arose about isolating patients and their contacts and about quarantining institutions or even whole cities or states. It was abundantly clear that strategies were uncertain and national, state, and local preparations were grossly inadequate.

Subsequent to the exercise, Senator Nunn stated that he was deeply troubled by what had been revealed and said that he would ask Congress to permit him personally to brief them on the dangers that the country faced and the need for resources specific to the need. This he did in special hearings.

A New Impetus -- the 2001 World Trade Tower attack and the anthrax outbreaks

On September 11, 2001 --only three months after Dark Winter, the attacks on the World Trade Center Towers and the Pentagon occurred. Two weeks later, letters containing anthrax were sent to members of Congress and news centers. In all 22 persons were infected -- 5 died. We feared that more attacks were imminent.

Secretary Thompson, then Secretary of HHS, created a new entity, an Office of Public Health Emergency Preparedness and a three billion dollar emergency appropriation was signed. Funds were to be made available to CDC, NIH, and the FDA; to state and local health agencies

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for such as community planning and development; for laboratories to create quickly accessible diagnostic services; for hospitals to prepare and exercise plans for dealing with large numbers of casualties; for epidemiologists to develop reporting and response systems.

Remarkable changes have occurred since John Bartlett convened the Symposium on "Bioterrorism" in September 1997.

Communication systems now link central command centers at national, state, and city locations; a laboratory network of more than 100 laboratories is capable of rapid diagnosis of many different biological agents; strategic national stockpiles of critical supplies and equipment can be dispatched with notice of only hours; all hospitals have emergency plans for dealing with a sudden influx of patients; surveillance networks have been established; plans are in place to muster large numbers of emergency personnel.

In many communities now, all hazards preparedness and response systems are becoming well established; others are still emerging. More needs to be done but a remarkable groundwork has been laid for more effective medical and public health responses to natural disasters as well as bioterrorism.

What of the future? With ever-increasing travel and rising densities of population, it can confidently be predicted that so-called emerging infections will steadily increase in number; that bioterrorists will be a greater problem what with more sophisticated laboratories, more extensive biological training, and more information on the internet. New respiratory epidemics such as SARS, MERSA, pandemic influenza will recur more frequently; Dengue and Chikungunya infections are on the march and now we learn of a spreading Ebola hemorrhagic fever of record size. New and better control methods, vaccines, antimicrobials, creative control strategies are more critical than ever. It is a new era for the infectious diseases.

From complacency to preparedness A salute to John Bartlett who dislodged the first stone of complacency and launched a landslide.

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Table Top Exercise at Andrews Air Force Base, June 2001

Key Participants

President	Sam Nunn
National Security Advisor	David Gergen
Director of Central Intelligence	R. James Woolsey, Jr.
Secretary of Defense	John White
Secretary of Health and Human Services	Margaret Hamburg
Secretary of State	Frank Wisner
Director, Federal Bureau of Investigation	William Sessions
Correspondent, NBC News	Jim Miklaszewski
Pentagon Producer, CBS News	Mary Walsh
Reporter, British Broadcasting Corporation	Sian Edwards
Reporter, The New York Times	Judith Miller

John Bartlett Symposium and Festschrift