Anthrax 2001 – Lessons Learned: Clinical Laboratory and Beyond

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OBJECTIVE: Re-visit the 2001 anthrax outbreak to assess the ideas and concepts learned from the event as they relate to the illness and to bioterrorism preparedness.

DATA SOURCES: Current literature.

CONCLUSION: A multitude of lessons have been brought to light. The future of bioterrorism preparedness depends on whether those lessons are acknowledged and acted upon.

ABBREVIATIONS: ASM = American Society for Microbiology; BT = bioterrorism; CDC = Centers for Disease Control; FEMA = Federal Emergency Management Administration; GAO = General Accounting Office; HHS = Health and Human Services; LRN = Laboratory Response Network; NCID/HIP = National Center for Infectious Disease/Hospital Information Program.

INDEX TERMS: anthrax; bioterrorism.

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***Focus Continuing Education Credit:** see pages 189 to 191 for learning objectives, questions, and application form.*

Do you remember where you were and what you were doing on September 11, 2001?

It is a day that will be frozen in memory for many. I was working at the bench in the microbiology laboratory of our city's largest hospital. The radio was tuned to the news as the horrifying details of the terrorist attacks on the World Trade Center and Pentagon unfolded. Questions entered my mind that seemed even more terrifying. What if the terrorists had carried with them organisms capable of infecting the populace of New York City and beyond? What if the deadly destruction created by the airliners crashing into the towers was just the beginning—to be followed by a sequelae of illness due to such BT (bioterrorism) agents as anthrax, smallpox, or plague? I was not alone in those thoughts. That same afternoon, CDC issued an official communication via the NCID/HIP Rapid Notification system.

> "ALERT: Terrorist Activity Response - Due to current events, CDC is on heightened alert status to monitor for any possible unusual disease patterns associated with today's events, including chemical and biological agents. CDC recommends that you initiate heightened surveillance for any unusual disease occurrence or increased numbers of illnesses that might be associated with today's events."

Fortunately, these fears did not materialize. Yet they served to elevate the awareness among laboratorians and clinicians for the possibility of a BT event. This heightened alert status was invaluable in rapid detection and identification as the lethal bullets of anthrax spores made their way through the mail system.

BT has been the topic of workshops, seminars, training sessions, colloquiums, audioconferences, and articles since 1999 when the CDC began widespread education to build the infrastructure of BT readiness. Healthcare institutions and laboratories have been encouraged to develop cooperative plans to deal with a BT event. Multi-disciplinary drills, such as Operation Topoff, involving experts from the FBI, FEMA, public health, law enforcement, emergency medical, and hospital staff have been carried out in various cities with critiques developed to remedy deficiencies in preparedness.[1] The anthrax outbreak was not limited to large metropolitan facilities. The lesson here is that every city or locale is at risk for involvement in a BT event. Every laboratory in every small town or large city has the potential of finding the index case of an anthrax – or plague, or small pox – outbreak. The statements "It won't happen to us" and "We are not a target" are dangerously naive. "Be Prepared" doesn't just apply to Boy Scouts.

The LRN has established the Level A laboratory as the sentinel of a BT event. These laboratories have been designated to 'rule-out' the most likely BT agents using basic and rapid laboratory techniques defined as Level A laboratory procedures. These procedures are readily available on the CDC and ASM websites.[2,3] In Palm Beach County Florida, both the on-site rapid response laboratory and the off-site main laboratory noted the unusual nature of their findings on CSF Gram stain. Their prior training in BT preparedness guided them through the appropriate steps necessary for prompt referral of the organism to their Level B laboratory where it was identified.[4,5] Nothing substitutes for adequate training. Training must be on-going and widespread, with money appropriated

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to facilitate education programs in all laboratories – from the smallest rural facility with minimal expertise in microbiology to the large metropolitan laboratory with abundant and experienced microbiologists.

The lack of communication between different agencies involved in preparation for and handling of a BT event has been a common complaint throughout the anthrax situation and during follow-up and critique of preparedness drills. In both the first case in Florida and the last case in Connecticut, the laboratory that initially isolated *B. anthracis* in cultures and forwarded them to the Level B public health laboratory, found out the identity of the organism through television news reports. The top-to-bottom communication system failed.[4,5,6]

In our own situation, local public health officials have not been active in communicating with hospital microbiology laboratories. Advance guidelines on how to handle questions from the worried well and from postal employees were non-existent. The CDC Website became our source for updates, recommendations, and protocols. Protocols detailing optimal specimens and specimen collection were taken directly from the Website and were printed and distributed to the emergency departments for inclusion in their BT preparedness guidelines. Practice drills and brainstorming sessions locally have involved law enforcement, FBI, emergency medical, fire department, and others but have not included hospital microbiology department representatives as an integral part of the team. When a microbiology supervisor did attend a session in November, 2001, she was able to share valuable information. The group had been unaware of the LRN and the role of the Level A laboratory. Nor were they aware that *B. anthracis* could not be identified definitively at the Level A laboratory. The lesson here is that expertise from all areas of involvement must be included in the planning and practice stages to have a complete picture of what a BT event may encompass.

Communication within and between facilities can also be a source of weakness. Our hospital system consists of three urban facilities and three hospitals that are located in smaller rural towns. The initial BT preparedness plan that was put together focused on the urban facilities with the thought that they would be the recipients of most of the phone calls, specimens, and patients. It was only a few days into the anthrax outbreak when that plan proved deficient. A near-panic call from the smallest rural hospital indicated that they were receiving questions from physicians as well as mail carriers and the worried well. A duplicate notebook of all the information that had been put together was forwarded to them and to the other rural facilities immediately. Updates are communicated to them as they occur.

Other communication deficiencies that have been noted include the difficulty that Level A laboratories have had in contacting a person-in-charge at their Level B facility on a 24/7 basis. Messages left on voice-mail were not returned in a timely fashion if at all. Level A laboratories often did not know where their closest Level B laboratory was. The Florida laboratory sent their *B. anthracis* isolate to Jacksonville some 300 miles away rather than to the Level B laboratory located in Miami only 25 miles away.[5]

There was no early guidance in the collection of nasal swabs. Public health provided no ammunition to deter the practice. Level A laboratories were frequently over-run with requests for this inappropriate culture. A newspaper article printed in our local paper included a diagram that showed using nasal swabs for isolation. Microbiology supervisors demanded – and received – a retraction of that erroneous information. Using CDC guidelines, we successfully adopted the 'just say NO' response to the request for nasal swab cultures.

Evaluation of the first ten confirmed cases of inhalational anthrax provided lessons in the areas of diagnosis through laboratory testing and radiology.[7] Blood cultures were positive in all cases (n = 7) when collected before the administration of antimicrobics. In those cases where antimicrobial therapy had already been given, PCR and/or immunohistochemical staining of sterile body fluids was required to confirm the presence of *B. anthracis.* ELISA serological quantitation of IgG anti-protective anthrax toxin antigen coupled with a confirmative inhibition assay also proved valuable in confirming infection. Productive cough was uncommon. This indicated the limited value of sputum culture and Gram stain for organism isolation. Rhinorrhea was also uncommon which helped in the differential diagnosis versus influenza and influenza-like illness (Table 1).[8] The presence of fever, chills, malaise, fatigue, nausea or vomiting, and chest discomfort in a majority of inhalational anthrax cases further aided in that differential. Abnormalities in the chest x-ray could be seen as soon as 48 hours after on-set of symptoms. This is in contrast to the generally normal chest x-ray found in influenza-like illnesses.[9,10]

New information regarding antimicrobial therapy of inhalational anthrax was another outcome of the outbreak. Historically, survival of patients with inhalational anthrax was unlikely. Limited information was available regarding treatment. Three patients who survived inhalational anthrax in the U.S. in the 20th century received penicillin plus streptomycin, tetracycline plus cephalothin, or penicillin plus chloramphenicol. There had been no clinical trials in humans. Susceptibility data derived from testing these isolates led to the current recommendations for treatment which includes the use of ciprofloxacin or doxycycline, plus one or two other drugs to which the isolate is susceptible. The isolates were resistant to cephalosporins and trimethoprim-sulfamethoxazole.

The value of preparedness has not gone unnoticed by government officials. The Kennedy-Frist bill, known as the Public Health Threats and Emergencies Act of 2000, aims to revitalize the nation's ability to monitor and fight outbreaks of infectious disease and

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protect the nation more effectively against BT.[11] The measure targets improving coordination among federal agencies responsible for all aspects of a bioterrorist attack. Included in the legislation is additional funding to train healthcare personnel to recognize BT agents. On January 10, President Bush signed into law the $2.9 billion BT appropriations bill. Just 21 days later, HHS Secretary Tommy G Thompson announced a $1.1 billion infusion into state BT preparedness.[12] Letters were sent to state governors detailing how much each state would receive to help them strengthen their capacity to respond to BT. The money will allow states to begin planning and building the public health systems necessary to effectively respond. Statewide emergency preparedness, the creation of regional hospital plans of response, and improvement of local city-wide response plans are all part of the new funding package. Critical benchmarks for BT preparedness planning include timelines for development of each level of planning, establishment of a bio-preparedness planning committee for hospitals, and development of a plan to improve working relationships and communications between Level A (clinical) laboratories and Level B/C laboratories and between hospital emergency departments, state and local health officials, and law enforcement on a 24/7 basis. Assessment of training needs of emergency department personnel, infectious disease specialists, public health staff and other health care providers is another benchmark critical to preparedness.

With continued emphasis on communication and education, the lessons learned from this small but deadly BT outbreak will provide the basework to ensure that America's ability to deal with BT is as strong as possible.

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Table 1. Symptoms and signs of inhalational anthrax, laboratory-confirmed influenza, and influenza-like illness (ILI) from other causes[8]

Symptom/Sign	Inhalational anthrax (n = 10)	Laboratory-confirmed influenza	ILI from other causes
Elevated temperature	70%	68% - 77%	40% - 73%
Fever or chills	100%	83% – 90%	75% - 89%
Fatigue/malaise	100%	75% - 94%	62% - 94%
Cough (minimal or non-productive)	90%	84% - 93%	72% - 80%
Shortness of breath	80%	6%	6%
Chest discomfort or pleuritic chest pain	60%	35%	23%
Headache	50%	84% - 91%	74% - 89%
Myalgias	50%	67% - 94%	73% - 94%
Sore throat	20%	64% - 84%	64% - 84%
Rhinorrhea	10%	79%	68%
Nausea or vomiting	80%	12%	12%
Abdominal pain	30%	22%	22%

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