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Grassley Seeks Improvements to Anti-bioterrorism Network

WASHINGTON – Sen. Chuck Grassley, ranking member of the Committee on Finance, today asked Homeland Security Director Tom Ridge to review expert critiques of the nation’s response to the anthrax attack last fall and make improvements as needed. Grassley’s letter to Ridge comes on the six-month anniversary of the opening of the anthrax-laced letter to Sen. Tom Daschle. Grassley’s letter to Ridge follows.

April 15, 2002

The Honorable Tom Ridge
Director, Office of Homeland Security
The White House
1600 Pennsylvania Avenue
Washington, D.C. 20502

Dear Governor Ridge:

Today marks the six-month anniversary of the opening of a letter containing anthrax to Senator Tom Daschle. The anthrax threat to postal workers and congressional staff in Washington, D.C., to media professionals in Florida and New York, and to two individuals in New York and Connecticut required a comprehensive, investigative response from various local, state and federal agencies. The unprecedented anthrax exposure prompted responding agencies to marshal untested resources. Given the newness of the situation, policymakers and public health experts must analyze the response, identify its strengths and weaknesses, and use the findings to inform future responses to similar threats and to circumvent tragedy.

I asked several public health experts to lend their expertise to this cause and provide a written critique of the local, state and federal agencies' response to the anthrax attacks. I asked them to comment on any aspect of the response as they saw fit, with an eye toward identifying strengths and weaknesses that could prove useful in the future. I also asked them to touch on, if they could, the interactions between responding agencies, including the Centers for Disease Control (CDC), the Federal Bureau of Investigation and the U.S. Army Medical Research Institute on Infectious Diseases.

Three of the experts provided critiques. They raise several points that highly concern me. For example, one expert feels the CDC failed to recognize that “a tape-sealed letter could leak (anthrax) spores.” Another expert believes the Federal Bureau of Investigation wrongly reassured the CDC that the anthrax had limited potential to spread. I am not in a position to verify these experts’ contentions, but I hope everyone in the public health community who dealt with last fall’s anthrax outbreak will consider these responses, analyze their relevance, and make any necessary changes to secure public safety in the event of another bioterrorism attack. Five people died in last fall’s anthrax outbreak. We have an obligation to them, to their families, and to the public to prevent any future loss of life.

Please let me know how your office processes these responses and ensures that the relevant agencies correct any applicable shortcomings. Thank you for your work to protect the public. Please call Jill Gerber of my staff at 202/224-6522 if you have any questions.

Sincerely,

Chuck Grassley
Ranking Member

Attachments: Critiques from Public Health Experts

TO: Senator Chuck Grassley
Senate Finance Committee
135 Hart Senate Building
Washington, DC 20510-1501

FROM: David S. Perlin, Ph.D.
Scientific Director
Public Health Research Institute
Newark, NJ 07103

DATE: March 17, 2002

RE: Evaluation of the CDC's response to the October 2001 anthrax outbreak

CC: John Drake

Executive Summary

The October 2001 anthrax outbreak resulted in 18 documented cases of disease with five deaths. More than 32,000 people were prescribed antibiotics, 10,000 persons were recommended to take at least 60 days antibiotic prophylaxis, and additional individuals with high-level exposure were offered a further course of antibiotic and the anthrax vaccine. Anthrax is not a new disease in the United States. It is endemic to some parts of the country and it is an occupational hazard in some industries. The CDC was faced with the task of managing the deliberate transmission of anthrax spores through the mail. The overall management of the outbreak was successful. But along the way, errors in judgment, poor communication, and a reluctance to modify approaches and outlook based on current findings led to the appearance of an agency that was not in full control. Most notable was the failure of CDC to recognize that a tape-sealed letter could leak spores. This was most serious because the spores emerging from those envelopes were potentially more deadly than those left behind. It was also surprising given the CDC's experience with previous threats of this nature. Furthermore, the CDC did not have a good handle on the surface properties of anthrax spores, which allowed them to adhere to mail and mail sorting machines, and be distributed through a complex mail system. Limitations on the use of nasal and environmental sampling were not explained to the public, which provided a false sense of security. Finally, assumptions about the infectious dose of spores required to cause disease and spore germination were too firmly cast in stone. Although morbidity and mortality was limited during this past outbreak, the lessons learned are critical to our ability to respond more successfully to future outbreaks.

Background

Anthrax cases: Rare but not absent

Bacillus anthracis is a spore-forming soil organism that commonly infects domesticated and wild animals, such as cattle, sheep, horses, mules, and goats. Humans become infected incidentally when brought into contact with diseased animals, which includes their flesh, bones, hides, hair and excrement. For this reason, anthrax has been a common source of disease in the textile industry, "Woolsorters Disease." It is found throughout the world causing sporadic and endemic disease. In the United States, areas of infection include South Dakota, Nebraska, Arkansas, Texas, Louisiana, Mississippi and California. Naturally occurring anthrax cases are uncommon but not absent in the United States.

Anthrax spores

The spore-forming characteristic of *Bacillus anthracis* has made it a desirable agent for biological warfare. Anthrax spores contain the genetic material of the bacteria encased in a tough protein coat. They are dormant and highly resistant to a variety of stress conditions including extreme heat and cold, ultraviolet radiation, and chemical treatment; they can retain viability in soils for more than 50 years. When environmental conditions are favorable, the spores germinate and develop into the disease-producing form of the organism. The *Bacillus* spores have surface properties that cause the spores to be attracted to one another, as well as to various solid surfaces. This well known property is a major hurdle in developing anthrax as an offensive weapon because clumping of spores results in large aggregates. Various substances, like bentonite, which neutralize surface charges on the spore, significantly reduce attractive forces between spores and promote relatively free dispersal. Since the start of offensive weapons programs in the United States and Soviet Union in the 1940s, it was presumed that a successful attack with anthrax would require the rapid dispersal of substantial

quantities of free spores in a so-called "weapons-grade" form. For this reason, it is generally assumed by specialists that suspicious powders presumed to be anthrax are of weapons-grade caliber and therefore contain freely dispersed spores. Such freely dispersed spores would be either individual spores in the 1-2 micron range or aggregated spores mechanically milled to produce spores in the same range. Such spores in sufficient quantities in the right host would be capable of producing the inhalation form of disease.

Disease pathology

Anthrax infection results in three clinically distinct diseases: cutaneous (skin), gastrointestinal and inhalation disease. Cutaneous anthrax is initiated when spores of *B. anthracis* are introduced into the skin through cuts or abrasions. Spores germinate within hours, and the cells multiply and produce anthrax toxin with ensuing edema and necrosis. Gastrointestinal anthrax occurs following the ingestion of contaminated meat. The bacteria move to mesenteric and other regional lymph nodes where they multiply and disseminate. The most feared of the three clinical states is inhalation anthrax. Normally, large clusters of anthrax spores (greater than 5 microns) are deposited in the upper airways (pharynx, larynx, and trachea) and are effectively trapped or cleared by the mucociliary system. However, small individual spores (1-2 microns) can reach the alveolar ducts and alveoli where they are engulfed by pulmonary macrophages and transported to mediastinal and peribronchial lymph nodes. Following germination, a large amount of anthrax toxin is produced. Edema factor and lethal toxin produced by the vegetative organism causes massive hemorrhagic mediastinitis that is typical of inhalation anthrax. Regional lymph nodes are quickly overwhelmed and the toxin enters the systemic circulation resulting in edema, hemorrhage, necrosis, septic shock and death.

October 2001 Outbreak Issues: CDC response

Mail as a vector for spore dispersal

Unlike bioterrorism-related exposures in Japan and the former Soviet Union, the US Mail system was used as a vector to spread disease in the October 2001 outbreak. The outbreak was almost certainly exacerbated by the CDC's slow recognition that anthrax could permeate a tape-sealed letter and that spores could effectively "hitch-hike" through the mail. The CDC's lack of preparedness for mail-based biological terrorism was surprising given their experience with previous threats of this nature. The CDC was fully aware that mail could be used as a potential vehicle to deliver fatal anthrax spores. From October 30 through December 23, 1998, CDC received reports of threats of anthrax-laden letters sent to health clinics in Indiana, Kentucky, and Tennessee, as well as a letter in California sent to a private business. All threats were hoaxes and were investigated by FBI and local law enforcement officials (MMWR 1999, Feb 5). Certainly, the CDC and FBI analyzed these letters for anthrax contamination and were aware of their potential to deliver anthrax spores. Most disturbing was the failure of CDC to recognize that individual anthrax spores, with a well-documented small spore size of 1-2 microns (e.g. Shafazand et al. 1999), could easily penetrate a standard cellulose-based envelope. The size of spores was well known because a debate had already emerged over the best type of particle respirator to use in the event of an attack (Nicaset al. 2000) or to protect workers in the textile industry (see http://www.3m.com/occsafety/html/anthrax_notice.html). Clearly, spore size and its challenges were a safety issue for some time.

If there was any question about the containment properties of an envelope, a quick call to paper industry experts or a simple search through the internet would have revealed that standard envelopes have numerous micro-channels of 5 microns or greater. Such channels not only serve as an exit point for anthrax spores but also serve as a selective filter to allow the smallest and most

deadly spores to be released while retaining the largest and least virulent clumps. High-speed postal equipment, which places letters under high pressure, further served to force spores through these openings. Thus filtered spores emerging from the so-called "sealed letters" resulted in large numbers of small, freely dispersed (unclumped) spores being deposited on mail machines, mail, and in mail rooms. The release of deadly free spores through an inadvertent pressurized filtering process may have accounted for the high degree of inhalation anthrax in postal workers, and for the deadly consequences of contaminated mail.

Anthrax and cross-contamination of the mail

Once it was known that anthrax was being distributed through the mail, it should have come as no surprise to the CDC that *Bacillus* spores could adhere to pieces of mail emerging from high-speed sorters. The sorters impart an electrostatic charge to the letters, which serves to attract the spores and hold them tightly. A great deal is known about environmental conditions and physical properties of surfaces that promote spore adherence (e.g. Husmark and Ronner (1990); Dragon, 1995; Ronner et al. (1990); Matz et al. 1970). The high-speed sorters and mail-processing units should have been expected to act as electrostatic generators, attracting and holding spores like magnets. It is for this reason that the spores were not released into the air until postal workers used high-pressure air to clean sorting machines. Once aerosolized, the spores became deadly. For this reason, cross-contamination of the mail from an initial inoculum produced by one or more spore-laden pieces of mail should have been expected. Tight adherence of spores to cross-contaminated letters could easily have allowed contaminated mail to be distributed through a complex mail delivery system, and could well account for fatal exposures of susceptible hosts such as 61 year-old Kathy T. Nguyen (New York City, NY) and 94 year-old Otilie Lundgren (Oxford, CT). If free spores were dislodged from the mail to produce a fatal dose, then it might be reasonable to expect that spores adhering tightly to the letters were more likely to be small and individual rather than clumped. This would be consistent with cross-contaminated mail resulting from freely dispersed spores (smallest and most deadly) emerging from the original letters after being filtered through micro-channels in the envelopes. Spores hitch-hiking through the mail by surface adherence is not surprising. The tight adherence of spores to other charged surfaces, such as protein in wool from imported raw fabrics, was a frequent cause of inhalation anthrax disease (Woolsorters Disease) in textile mills in the 1940s and 1950s (Gold, 1955). Clearly, tightly bound spores can be dislodged and cause disease. Approximately 85 million pieces of mail were processed on the days after the implicated envelopes passed through the NJ and the District of Columbia (DC) sorting facilities until they were closed. Both of these facilities had evidence of widespread environmental contamination with *B. anthracis*. Certainly, anthrax spores were moving in many directions.

Spores are everywhere

Once released, *Bacillus* spores will move rapidly through air currents and contaminate extensive exposed surfaces. Offices, lab complexes (e.g. Fort Detrick's infamous Building 470) or even whole islands (e.g. Britain's Gruinard Island) can be extensively contaminated following high-level exposures. The CDC recognized quickly that HVAC systems and nearly all surfaces had the potential to be contaminated. Academic researchers, especially those engaged with tissue culture, know that spore-forming organisms like *Aspergillus* are a nightmare to contain. Entire buildings can become infected from a single lab engaged in routine experimentation. Thus, it is not at all surprising that a letter leaking spores could contaminate thousands of pieces of mail, nearly all exposed surfaces, and could be carried into buses, cars and homes by workers with inadvertent exposure. Environmental sampling results in this investigation indicated widespread contamination from the letters processed for delivery to the offices of two U.S. senators. Although sampling with surface wipes has been the

standard sampling method and has advantages for sampling some small surfaces, surface wipes have several limitations. Wipe samples might miss minimally contaminated surfaces or smaller, discrete contaminated areas. In fact, some confusion arose early because some simple wipe tests were negative, while a more thorough use of HEPA filtered vacuum sampling was positive. This reflected the ubiquitous nature of dispersed spores and either their tight adherence to certain surfaces or inadequate sampling material used in the environmental swabs.

In order to certify that Senator Daschle's office in the Hart Senate Office building was clean, several thousand surface samples were taken. This was probably a prudent measure given the unreliability of routine environmental swabs to detect anthrax from surfaces known to be exposed. However, far fewer swabs were taken from postal facilities. For example, when tracking down cross-contamination of the letter(s) believed to be responsible for infecting Mrs. Otilie Lundgren in Connecticut, only 117 samples from the Wallingford facility, 29 samples from Seymour facility, and 43 samples taken at Lundgren's home were used to declare those building free of anthrax. When dealing with trace amounts of a biological agent, more samples, not fewer, relative to a large exposure are needed. How does the CDC reconcile the number of samples taken from those facilities, and others, with that of the Hart Building? If they know more now, have they gone back and re-sampled those facilities? Has the EPA been involved with those facilities?

Nasal sampling and surface wipe tests

Early in the anthrax outbreak, nasal swabs were being used as an indicator of human exposure to aerosolized anthrax spores. While the intent was right, it became clear quickly that this methodology was highly flawed and was not a reliable predictor of exposure. Several of the individuals that died from inhalation anthrax had negative nasal swabs. The CDC readily acknowledged that a negative nasal swab did not mean that a person was not exposed. "Nasal swab cultures should not be used to diagnose cases of anthrax or to evaluate whether a person had been exposed" (MMWR 2001 Nov. 9). Nasal swabs can occasionally document exposure, but cannot rule out exposure to *B. anthracis*. As an adjunct to epidemiologic evaluations, nasal swabs may provide clues to help assess the exposure circumstances" (MMWR 2001 Oct. 26). If nasal swabs were of marginal value, then why so much emphasis on them and why wasn't the limitation of this test publicized more readily. More than 5000 nasal swabs were taken from employees at the Hart Senate Office building, which had extensive anthrax exposure. Nearly all were negative. The CDC regularly reported that workers suspected of exposure had negative nasal swab tests suggesting that they had no exposure. In fact, the nasal swab test is unreliable at best. Given the affinity of anthrax spores for protein in hair, it is surprising that hair sampling was not used as a better indicator of environmental exposure. Human hair presents a far greater surface area than the nose and does not have clearance systems operating to cleanse mucosal surfaces. Surgeons know far too well the potential for hair to retain airborne microorganisms. Why wasn't this approach used? It is difficult to believe that CDC did not consider this possibility. The October 2001 outbreak was a perfect time to evaluate the effectiveness of such a sampling technique. In the end, a highly flawed sampling methodology remains the only option for a new outbreak.

How many spores are needed to cause inhalation anthrax?

In the early phase of the outbreak, the CDC maintained that the "textbook" infectious dose of anthrax required to produce inhalation disease was at least 8,000-12,000 spores. For this reason, as spores were detected in offices, workers were told that the number of spores detected fell below the threshold level required to cause disease. However, as the outbreak continued two fatal cases of

inhalation anthrax and a case of cutaneous anthrax were documented in which there was no direct evidence of any spore exposure. The most likely explanation was incidental exposure through cross-contaminated mail or other environmental sources whereby small numbers of spores caused disease. It should be recognized that several academic researchers, myself included, publicly challenged the threshold value because of the way it was derived. An infectious dose has never been established for humans. Rather, the number was inferred indirectly from animal model studies and from an evaluation of human disease documented in U.S. textile mills and through naturally-occurring outbreaks and deliberate (accidental?) releases such as in Sverdlovsk in 1979.

Published lethal doses of anthrax spores that cause 50% death (LD50s) range from less than 10 spores for the guinea pig, 3,000 for the rhesus monkey, 1,000,000 for the rat, 1,000,000,000 for the pig and 5,000,000,000 for dog (Watson and Keir, 1994). LD50s in non-human primates range from 2,500 to 760,000 spores (Meselson et al., 1994; Watson and Keir, 1994). It is generally assumed in humans that substantial exposure was necessary before the risk of inhalation anthrax becomes significant. However, in Namibia, where anthrax is epidemic, a recent study found that the highest levels in air sampled downwind from disturbed dry, dusty anthrax carcass sites were 20 to 40 colony-forming units of spores per cubic meter. It would take about 2.5 minutes for an average human undergoing moderate activity to inhale 1 spore (Turnbull et al., 1998). It was suggested that such levels would be unlikely to contribute to infection. Yet disease is prevalent in the area. This may indicate that either a smaller dose can cause disease or inhaled spores are accumulating with time.

The likelihood and severity of an infection depends on multiple factors including route of infection, nutritional and other health states of the host, and relative virulence of the infecting strain. It should also be recognized that infectious doses generally follow a bell-shaped curve in which most people fall on the flat portion of the curve. In essence, the majority of cases will require a broad minimum and maximum range of spores to cause disease. However, a much smaller population will develop disease following exposure at the extremes of the bell curve, representing low and high spore levels. The implication of such an infection model is that in order for several individuals to have contracted inhalation anthrax without documented exposure, small numbers of spores were most likely involved and many thousands of people had to be exposed. The CDC reluctantly acknowledged this inevitable conclusion in late December 2001 following months of denying this possibility. It was this recognition that placed an additional burden on the EPA to clean-up "every last spore" in the Hart Senate Office Building. While the textbooks were mostly right, the CDC failed to recognize that a subset of the population was highly susceptible to infection. In addition, they were too slow to modify their risk assessment for a spore threshold for active disease. In light of the CDC's current position on the dangers of small numbers of spores for certain populations, such as immunosuppressed elderly, chemotherapy or HIV patients, have they re-tested postal facilities or other buildings deemed safe because they were below the previous spore threshold for causing disease?

Spore germination: incomplete assumptions.

The original decision to provide 60 days of antibiotic prophylaxis following potential anthrax exposure was based mostly on case emergence in outbreaks, so-called epidemic curves. However, little or nothing is known about spore latency (delayed germination) in humans. In some diseases, such as tuberculosis, where microorganisms are also taken up by macrophages in the lungs, latency may be months or years. There is no definitive data in humans. In model animal systems, factors affecting spore germination have been extensively studied (Titball et al. 1987; Guidi-Rontani et al. 1999). Numerous host conditions will impact spore germination. Like TB, immunosuppression may be an important factor. In addition, the affects of antibiotics like ciprofloxacin or doxycycline on

spore germination in a prolonged exposure model has not been addressed. Some 32,000 people were prescribed antibiotics for 60 days and probably hundreds of thousands of people took antibiotics as a prophylactic measure. These considerations forced CDC to acknowledge after the 60 day period expired that individuals with suspected exposure were still at risk. In addition, CDC offered that spores could be detected in the lungs 100 days following exposure. They then recommended an additional course of antibiotics and or investigational use of the anthrax vaccine as a post-exposure prophylactic. Why did it take so long to inform the public about the uncertainty of the germination time. In this outbreak, short-term latency was not observed. Many, perhaps thousands of people were exposed to anthrax spores at some level. These people are not sick. But, it would not be surprising in the future to see one or more cases of inhalation anthrax resulting from latent spore germination because an infected host's immune status has changed. Time will tell.

Identifying anthrax in clinical and environmental samples: more obstacles.

A definitive diagnosis of anthrax requires culturing of live organisms from specimens such as blood, tissue, exudates, sputum and environmental surfaces. Certain immunological and biochemical tests are available to confirm the identification once an organism grows, usually after 12-24 hours. Final testing requires several days for confirmation. Molecular-based polymerase chain reaction (PCR) techniques can be used to rapidly identify the organism. PCR analysis is fast, often producing results within hours. Yet, PCR alone can be unreliable (MMWR December 7, 2001). However, when coupled with state-of-the-art probes such as TaqMan, Light-cycler or Molecular Beacons, PCR is not only fast, but nearly 100% accurate. The CDC developed such an approach several weeks after the initial outbreak. But they have systematically refused to provide non-infectious reference DNA to state health departments or academic labs seeking to develop alternative strategies. PCR-based approaches are not only essentially because they are fast, but they can also be developed in a high through-put automated capacity. Such an approach is critical for analyzing numerous (thousands) environmental samples from a suspected outbreak in a timely fashion. Without such approaches, health department labs will be overrun with samples in short time in a future outbreak where multiple sources occur.

Vaccination: a good decision not well received

Approximately 10,000 persons potentially exposed to anthrax in Connecticut, Florida, New Jersey, New York City, and Washington, D.C., were recommended to take at least 60 days of postexposure antibiotic prophylaxis. Those with high level exposure are eligible to receive the anthrax vaccine (MMWR 2002, Jan. 25). But public health officials have a perceived credibility problem created by a well-documented series of miscues in the anthrax outbreak of the past few months. The abrupt change in thinking about spore persistence and germination, and the potential future health risk prior exposures posed, has eroded the public's confidence in health officials to properly guide management of a deadly disease. To further complicate matters, the use of the anthrax vaccine was being described as experimental, falling in the category of an investigational new drug (IND) requiring informed consent of patients. This was necessary because the vaccine is not FDA-approved for prophylaxis following pathogen exposure. Patients would be advised to consult their primary care physician for guidance and monitoring of side effects. In an atmosphere already consumed with doubt about the CDC's knowledge about anthrax and the nuances of its health risks, the public reacted with skepticism over the latest CDC recommendation. A vaccine is almost always preferred over antibiotic prophylaxis when considering side effects and the loss of an antibiotic class through emergence of drug resistance. At a different time, perhaps even six months ago, a controversial recommendation from the CDC would have been well received. But public confidence

has been shaken during the latest public health emergency. Too often statements of fact were retracted or qualified weeks or months later. This is truly an unfortunate turn of events because a beleaguered CDC made the right decision. An assertive preemptive approach utilizing a vaccine is the best way to protect the public's safety. Yet, the public has not embraced the CDC's view. To many, it requires a leap of faith to embrace such an approach given their shaken confidence. A small number of federal employees did agree to take the vaccine. But many balked. D.C. Mayor Anthony Williams flatly recommended against the vaccine citing side effects and a lack of clinical data to support its use. Similarly, William Smith, President of the New York Metro Area Postal Union rejected the vaccine as a solution to lingering spore counts at the Morgan postal facility in New York and demanded that the facility be thoroughly cleaned and tested.

In principle, the anthrax vaccine should be safe. Unlike other types of vaccines, it does not use killed organisms to induce immunity. Rather, it is a subunit vaccine consisting of a culture-purified protein, "protective antigen," as the principal determinant of immunity. Limited clinical data, mostly in the textile industry, supports its value in preventing disease. Even though local minor reactions at the injection site are observed in 30% of the people that receive the vaccine, serious side effects are rare. In a comprehensive review published in the CDC's MMWR, 1,859,000 doses of the vaccine were distributed in the United States from January 1, 1990 through August 31, 2000 (MMWR 2000 December 15). During this period, 1544 adverse events, those requiring medical attention, were noted but only 76 were deemed as potentially life threatening. As vaccines go, the safety profile appears quite good.

So why the outcry? First, the public was concerned about substituting one risk, anthrax exposure, for another, vaccine-related complications. Second, the anthrax vaccine has been linked by some advocacy groups to the multisymptom "Gulf War Syndrome." Although epidemiological data does not support this linkage, many remain skeptical. In October, 2000, the General Accounting Office stated that 25 percent of the 176,000 pilots and crew in the US Air Force and Air National Guard left their jobs or asked to be reassigned to avoid anthrax vaccinations. Third, the sole U.S. manufacturer of the anthrax vaccine, BioPort Corporation (Lansing, Michigan), has had consistent quality control issues related to the vaccine production. The FDA only recently reinstated the manufacturer. In addition, the FDA complained in the past that reports of adverse reactions to the vaccine from members of the armed services were not being tracked or investigated by BioPort, as required. These lingering issues have cast a cloud over the anthrax vaccine program. Regrettably, public health officials have not adequately addressed these issues, which has further eroded the public's confidence. Public confidence in the CDC may be shaken, but their leadership is needed now and in the future. They should press forward with this difficult decision in a firm and decisive manner. If safety questions persist, then they should be addressed openly.

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3/13/02

Senator Charles Grassley
Ranking Member
United States Senate
Committee on Finance
Washington, D.C. 20510-6200

Dear Senator Grassley,

Thank you for requesting my analysis on the handling of last Fall's bioterror crisis. I will direct my comments to the official response and its relevance to future threats.

The anthrax mailings revealed a lack of integration among the various agencies that were called upon to defend against the threat. Specifically, the FBI led the investigation, and acting with strict criminal protocol, conducted experiments using the USAMRIID lab, but excluded CDC scientists from directly examining the envelopes.

Nor did the Army perform the appropriate tests right away; in fact DNA tracers to check seepage from the envelopes, and quantitative tests to determine airborne potential, were not conducted until late October, when several people had already gotten sick and two had died.

The CDC, in turn, spread faulty information to the local health agencies and the US Postal Service based on epidemiological speculation. Not seeing the evidence, and being wrongly reassured by the FBI, the CDC guessed that the anthrax had limited potential to spread. Then when the two postal workers died in Brentwood, the CDC overreacted, not by closing facilities, but by administering antibiotics to 30,000 postal, media, and government workers who were anywhere near where the anthrax had been found. This overuse of antibiotics (only eighteen people actually acquired anthrax overall), caused needless expense (millions of dollars), and side effects from the medication (diarrhea, insomnia, rashes).

The antibiotic authorized for use, Cipro (\$300 for a month's supply), is ten times more expensive than generic equivalents (doxycycline - \$30 for a month's supply) that have been tested and found to be equally effective against the anthrax bacillus. Examination of the anthrax itself revealed no drug resistance to any of these antibiotics, yet the more expensive Cipro continued to be used.

The FBI only showed photos of the anthrax letters to the CDC's scientists and epidemiologists. No one from the CDC examined the actual envelopes that were sent to Tom Brokaw, Senators Daschle and Leahy, and the NY Post. The Army Infectious Disease lab, which has the same top level D clearance as the CDC lab, had control of the letters. But the Army lab is oriented to biowarfare whereas the CDC targets public health. According to CDC's Deputy Director for Infectious Disease, Julie Gerberding, the Army worked directly with the FBI, and the CDC was informed of the results by conference calls organized by the National Security Council. At first the Army downplayed the risk to postal workers and the media, and the CDC relayed this reassurance.

On October 15th, the letter to Senator Daschle was received in his office and opened by his assistant. According to Dr. Gerberding, Army scientists did note that the anthrax in the Daschle letter had "a high concentration of spores, and that the powder would poof, indicating it was easily aerosolized and could float around in a more dangerous way." Yet the FBI continued to relay that the letter had been well sealed, only a risk to the person who opened it, (though only Daschle's assistant had seen it unopened), and therefore none of the other agencies including the CDC and the Postal Service expected the anthrax to escape the envelope.

It was only after workers got sick that the CDC began closing government buildings and postal facilities, and under pressure from the media began to hand out antibiotics to everyone who was in a contaminated building. The initial underreaction was followed by a costly overreaction. This anthrax was deadlier than expected, but it was still not contagious and the mail was an inefficient way to spread it. In the end, many more people probably got sick from taking Cipro than from anthrax.

Had the FBI integrated its team with the Army and the CDC, had this team worked together with state and local agencies, the reaction to the anthrax could have been earlier, more appropriate, and more to scale.

Deborah K. Willhite, Senior Vice President of the Postal Service for Government Relations, in a letter to you dated November 14th, wrote that the Postal Service "received critical information through the media, not from other agencies. The different focuses of various law enforcement and health organizations resulted in parties speaking different languages. And, absent an established protocol, lines of authority could be unclear."

Even after a postal task force was organized, the CDC only provided guest experts, and was no direct input to the Postal Service from the FBI.

Here in New York, state and city health departments relied on the guidance and the presence of the CDC. Resources were marshaled to test large numbers of the population, without knowing whether this would be necessary or not. Labs were readied to perform nasal swab testing of all who might be exposed to anthrax, and blood cultures on those who might already be sick with inhalation anthrax. (the blood cultures could help distinguish anthrax from flu). At first, nasal swabs were felt to be adequate screening, until the CDC reversed itself in late October and indicated that the test was useful for epidemiological purposes only. But the NY State epidemiologist, Dr. Perry Smith, told me that nasal swabs did in fact have clinical value if it detected the presence of anthrax - whereupon treatment could potentially prevent the onset of the disease.

The confusion about testing; who to test, how to test, how many to test, typified the lack of knowledge and the lack of communication between the CDC and the local agencies it was asked to inform. This problem would have been less significant if the CDC had seen the anthrax and been better able to make predictions about its potential for spread.

Going forward, if a team of experts in public health is integrated with a team of nose-to-the-ground law enforcement agents, the result could be a tight web of educated defenders. In fact, Dr. Mitchell Cohen, the CDC's Director of Bacterial Diseases and liaison to the FBI, admitted to me that these "different cultures are not used to working together," but that a partnership is crucial to fight bioterror. He said, "we will be going to FBI headquarters. Our different approaches can complement each other. We look at information in different ways, Scientists collect data, develop hypotheses, and test them. Law enforcement examines the data for patterns to develop leads. One side might find what the other side is missing."

Now that 11 billion dollars has been budgeted to protect the public against future threats of bioterror, consideration must be given to where the money will be spent. Antibiotics, vaccines, and beefing up state and local health care agencies are considered primary targets for the funding. But the

real protection against bioterror, the safety net that can be built of epidemiologists, scientists, and co-operating federal agencies, has still not been established. And massive stores of antibiotics and vaccines are perishable, if not used within a few years, they will have to be discarded

Recently, truckloads of antibiotics were sent to Salt Lake City to cover the Olympics. Given how difficult it is to spread anthrax, those antibiotics were due to be wasted, and now, after they expire in two years, discarded. Bioterror money is better spent in integrating agencies and in making sure an atrocity the magnitude of crop dusting a stadium doesn't happen. A more effective public defense against bioterror attack would be public education rather than antibiotics. Conferences and lectures could be given informing doctors and the public about tools of bioterror. A relevant medical data base that could be drawn from in the event of an impending attack would be worth the money spent. Accurate information about smallpox, other viruses, anthrax, plague, could go a long way towards calming fears and preparing a defense.

I believe large scale purchases of antibiotics should be avoided. For one thing, antibiotics convey the message that bioterror may be in the offing. For another, since a bacteria cannot possibly spread to thousands of people overnight, such a display of drugs is purposeless. Mass stores of antibiotics without the doctors ready to prescribe them for a disease that doesn't currently exist is a significant waste of funds. As was evidenced last Fall with the anthrax scare, public perception of a potential catastrophe can easily necessitate an additional expenditure just to combat hysteria.

Money is better spent on scientists, epidemiologists, and liaison services between federal and local agencies. The best return for the money would be in establishing a framework of expertise that could be mobilized but could also be used to reassure the public. But integrating agencies requires a spirit of co-operation. More than that there must be a structure, a designated bioterror agency under the auspices of the Office of Homeland Security with power over all the other agencies on issues of bioterror.

Though the FBI controls its turf and is not used to co-operating except on its own terms, still, I believe interagency liaison and the formation of a bioterror agency would be a good place to start when considering how to spend the money that's been allocated. A good epidemiologist or public health oriented microbiologist working in conjunction with an on-the-scene FBI agent might know exactly when a particular group of citizens is at risk. A suspected pathogen of bioterror could be subject to meticulous measurements to quantify its risk of spread. Vectors such as envelopes could be scrutinized with DNA probes to make exact predictions. Found spores could be sent right away to spore specialty labs. The information acquired from careful CDC supervised experiments could then be spread responsibly to states and counties perceived to be in danger.

Just assigning millions of dollars to a particular region will by no means assure that the response there is effective or integrated. Whereas a response team of high priced scientists would be worth the money spent.

Respectfully submitted,

Marc K. Siegel, MD
Asst. Professor of Medicine
NYU Medical School

February 26, 2002

Senator Chuck Grassley
U.S. Senate

135 Hart Senate Building
Washington, D.C. 20510

Dear Senator Grassley:

I am responding to your request of January 25 to critique the response by government agencies to the anthrax bioterrorism event that began in September 2001. As a former epidemiologist on the staff of the Centers for Disease Control and Prevention (CDC) for thirty-two years, I was in charge of the anthrax activities during the 1950s, 1960s, and 1970s and am acquainted with anthrax as well as with the responsibilities that CDC has been given related to bioterrorism. I am also well acquainted with the Epidemic Intelligence Service (EIS) that I directed for 11 years while at CDC. My comments are based on information from CDC's Morbidity and Mortality Weekly Report (MMWR), reports from various media sources, and by attending meetings both in Atlanta and in Washington, D.C. I feel that I can respond to your queries with objectivity.

Several years ago CDC had been given responsibility for developing a response plan for bioterrorism to be implemented at all levels of government i.e. federal, state, and local which in my judgment they carefully accomplished. It was previously acknowledged that CDC would be the lead federal agency in directing the public health response to a bioterroristic event. This was not what happened. There were problems with the release of information for the public and in conducting some of the field investigations. Whereas, CDC's normal actions would include daily public briefings reporting the current data developed from the investigations, it was reported that all briefings would come from Washington. One result of the inability of CDC to put out daily briefings was that state health departments were unable to obtain up to date information about the investigations. When information was released from Washington, it was not always correct information due to unfamiliarity with anthrax and with all the investigations in progress. When CDC wished to investigate certain potentially contaminated environments, they were told to stand aside, as others (the FBI) would be in charge of that activity. In determining the degree of environmental contamination of various buildings, CDC's expertise was not found useful, which resulted in confusion and inappropriate statements.

These are examples that I am aware of, when CDC's leadership was subverted. Initially data developed by other agencies were not shared with CDC, and yet CDC was supposed to make recommendations for control and prevention. If there is a criminal element to a bioterroristic event, then the Federal Bureau of Investigation (FBI) will be involved which is appropriate. It is obvious that the FBI needs to work with a certain amount of secrecy in order to conduct the criminal investigation in the manner in which they have expertise. However, CDC is sensitive to their public health responsibilities to keep the public aware of what is being done to try to determine the causation factors in a bioterroristic event and to help alleviate the fear and hysteria that is associated with such an event. But when they are not able to provide daily briefings, those who look to CDC for information will be frustrated, as was the case in this event. From what I observed, the relationship between CDC and the U.S. Army Medical Research Institute on Infectious Diseases was collaborative, cordial, and very important.

CDC, with its primary mission to control and prevent disease, with a dedicated, competent, experienced staff that is ready to travel on a moment's notice must be given the authority to operate as it always has in times of emergency. To put dampers on its actions, can only lead to problems, and I suggest this is what led to some of the problems that occurred during the recent bioterroristic event.

I was concerned over several problems within CDC. It appeared that there was no one person at CDC who was directing all of CDC's activities. Though they held daily meetings within CDC, no one person was fully knowledgeable about all of the activities in progress nor the results of various field and laboratory investigations. CDC did place some of their staff as liaison persons in cities of major involvement, but these persons were not always adequately informed of the current investigation data.

Use of a retrospective scope is dangerous. We must not forget that this is the first such major bioterroristic event to occur in the United States. No matter how carefully plans are developed for handling bioterroristic events, once an event has occurred, and the plan is implemented, problems will be identified. Each bioterroristic event will differ from a previous such event and it is not possible to foresee what will happen. Thus flexibility has to be part of any plan directed at reacting to a bioterrorist event.

It has been said that CDC did not advise the postal service early enough about the dangers of processing contaminated mail. Since this was the first known actual use of the mail to distribute B. anthracis, who would have thought that the environment in post offices could become contaminated from processing these letters. Also, CDC was not in charge of culturing the environments of the post office and of the government buildings so they did not immediately have all the necessary data upon which recommendations should be made. Some of the results reported by other agencies were of culture results from unproven field kits, whose sensitivity and specificity had not been determined.

The current bioterroristic event has clearly pointed out the significant need CDC has for additional resources. It has been reported that some new monies have been made available to CDC so that it will now be possible for the Epidemic Intelligence Service to be expanded in order that there may be EIS officers located in every state health department and in some of the larger municipal health departments. EIS officers represent the first line of involvement in investigating bioterroristic events. It is important that the support staff for the EIS officers also be expanded and given permanent status.

The fabric of CDC needs to be strengthened and expanded. The original buildings are old and need refurbishing. They have been forced to rent additional facilities throughout northeast Atlanta and this leads to inefficiency in operation as a team. CDC has developed plans to upgrade their current facilities and to build additional offices and laboratories on their current two primary sites, but this overdue development should be expedited so that it can be completed within five and not ten or fifteen years. The current facilities are an embarrassment and inhibiting especially when CDC is being given important new bioterrorism prevention responsibilities. If the government is serious about strengthening our ability to adequately respond to such events, there needs to be better support for the prevention activities and this should be given immediate and primary attention.

Education and training are an important aspect of bioterrorism preparedness and to this end CDC has developed plans for constructing a cutting edge training center on their primary campus in Atlanta.

This facility should be given the highest possible priority so that training both within the facility as well as for developing and implementing a full range of distant learning activities can provide as soon as possible.

Once the physical facilities and program strengthening actions have been taken, it will be apparent that the practice of prevention in general will be strengthened. Not only will we improve our ability to handle a bioterroristic event but many public health prevention programs will also be strengthened.

It is also necessary that CDC have the necessary authority and financial support to conduct research appropriate to their mission, which is control and prevention of disease whether it is related to bioterrorism or natural phenomenon. This includes operational research, which is exceedingly important for the vitality of their activities.

It is unfortunate that it takes this type of an event to emphasize the additional needs of support for CDC but let us not dwell upon the traumatic nature of the bioterroristic event but on the opportunity to have learned what deficiencies there are in the system so that corrections can be made prior to the next bioterroristic event. No matter what we as a country or what specific agencies do, we cannot prevent bioterroristic events but we can certainly reduce the quantitation of that event by being prepared to respond. This is the responsibility of CDC and I do hope that the resources will be made available to them so that they can operate in the manner in which they are well suited to function in these critically important emergency situations as well as during normal times.

I hope you find these comments useful.

Sincerely,

Philip S. Brachman, M.D.
Professor, Emory University

PSB/mjc