Webcast Transcript

Anthrax: What Every Clinician Should Know, Part 1

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Dr. Ed Baker (moderator):

Hello, I'm Dr. Ed Baker. I serve as director of CDC's Public Health Practice Program Office, and I'd like to welcome you to this special Public Health Training Network program on "Anthrax: What Every Clinician Should Know." We are broadcasting today from the headquarters of the Centers for Disease Control and Prevention and the Agency for Toxic Substances and Disease Registry in Atlanta, and doing this program in collaboration with our partners at the American Medical Association and the American Hospital Association. Participating today are physicians, nurse clinicians, and other healthcare providers, and many other colleagues working in a variety of settings and communities throughout the country. We appreciate your interest in what has become an important topic for us all, and anticipate that today's program will help to ensure successfully coordinated efforts between the medical community and public health practitioners in addressing suspected anthrax exposures.

As you have read in the program fact sheet, the goal of this program is to provide physicians, nurse clinicians, and other healthcare providers working in private offices, hospitals, and public health settings with an update of how to correctly recognize, test, diagnose, treat, and report cases of suspected anthrax exposure. To accomplish this, we have 3 main objectives for this program. First, to describe the critical role the front line medical practitioners play as an independent and essential part of the public health system surveillance of anthrax exposure. Secondly, to describe the proper clinical practice for early recognition, testing, diagnosis, treatment, and reporting of anthrax exposure. And finally, to provide accurate and relevant information about anthrax and the risk it poses to individuals and the community.

We have the pleasure of having with us today the Honorable Tommy Thompson, Secretary of the Department of Health and Human Services. Secretary Thompson will speak to us first, followed by Dr. Jeffrey Koplan, Director of the federal Centers of Disease Control and Prevention and ATSDR. We have with us CDC staff members Dr. David Stephens, Dr. Bradley Perkins, who will then present an overview of clinical guidelines and procedures for the early recognition, testing, diagnosis, and treatment of this condition.

Before we begin, we would like to express CDC's gratitude to key sponsors that have made this program possible: the American Hospital Association, the American Medical Association, the University of North Carolina School of Public Health. I'd also like to thank the many public, private, subscriber, and military networks that are assisting us in making this program available across the nation. Thanks to all of you. And now we would like to hear from Secretary Thompson.

Secretary Tommy Thompson:

Hello. Who is on?

Dr. Baker (moderator):
Secretary Thompson, this is Dr. Ed Baker at CDC with Dr. Koplan and Dr. Stephens and Dr. Perkins.

Secretary Thompson:
Wonderful.

Dr. Baker (moderator):
And we are broadcasting live to our network.

Secretary Thompson:
Well, that's wonderful. First, let me thank you all at CDC for the job you are doing. Can I start out and then turn it over to you, Jeff?

Dr. Jeff Koplan:
Absolutely.

Secretary Thompson:
Okay. Are the doctors and the hospital associations both on the line?

Dr. Baker (moderator):
Yes, sir.

Secretary Thompson:
All right. Good afternoon, everyone. I am very pleased to be with you today and I certainly appreciate the leadership that all of you on this teleconference have taken on this very critical issue. I first want to thank Dick Davidson of the American Hospital Association, who has issued a wonderful call to action in which he has urged all of you to both get back to work and also care for the needs of patients as you continue to wrestle with illness and disease. To me, it is exactly the right tack to take, Dick, and I thank you for it, and the hospital association, I commend you for carrying it out. The American Medical Association, I believe, has put out some tremendously helpful information on disaster preparedness and anthrax information. Both of your organizations who are on this teleconference call this afternoon, I appreciate it and thank you for taking your time out to hear from CDC and myself as Secretary. I believe you are both organizations that are doing outstanding work.

The Department of Health and Human Services, which is the agency which I lead, is the lead federal agency for the public health response to any biological or chemical attack. We are working vigorously with our federal partners to coordinate domestic preparedness, and I believe we are doing as good a job as can be under the circumstances, and I hope to continue to do so with your support and partnership.

We moved the bioterrorism preparedness efforts into my immediate office upon my being

selected as Secretary of Health and Human Services. I appointed Dr. Scott Lillibridge of the Centers for Disease Control, one of the nation's leading experts on bioterrorism, to head the Office for National Security and Bioterrorism. His office is on my floor in the HHS building right across from my office. I have also assembled a team of experts from throughout the Department of Health and Human Services and other federal agencies that are working 24 hours a day, 7 days a week in a conference room a few steps from my office to coordinate the intel that is coming in, as well as the department's activities in responding to the public health needs. I announced several weeks ago that I was creating an advisory committee that was going to be headed by Dr. D.A. Henderson (as all of you know, he is the physician who led the successful fight to eradicate smallpox), and he is on board almost on a daily basis. The president has now requested an additional 1½ billion dollars to combat terrorism to strengthen our ability to prevent and respond to a bioterrorism attack. The request is, of course, more than a sixfold increase of the current budget. A big share of that is going to be for the purchase of pharmaceuticals, namely the antibiotics that deal with anthrax but also 509 million dollars to speed the development and purchase of 300 million doses of smallpox vaccine.

We are going to also add 4 more push packs to the current 8. We have 400 tons of pharmaceutical supplies right now. This will raise it by an additional 200 tons and we will then be able to have even closer response time to locales throughout the country. We are also putting in 88 million dollars in partnerships to assist at the local level and to strengthen laboratory analysis, as well as to strengthen the local needs, which of course I think have been largely underfunded for several years. I also believe (and I've asked Congress—this is my request, it's not the president's, and not in the president's package), I have also requested that at least one federally funded epidemiologist who has graduated from the Epidemiology Intelligence Service Training Program at CDC be placed in every state health department and every regional office. We are also putting an additional 50 million dollars in to strengthen our metropolitan medical response system, and we will go from 97 communities to 122. These are the things that I think are pertinent to our discussion today, but I know that you have questions that you may want to ask of me, or more particularly and probably more importantly, of that of CDC led by Jeff Koplan. I would like to just add that I think CDC has just done an exemplary, fine job throughout this whole thing. I can't tell you how much I appreciate their support and partnership and the professionalism by which they have conducted their work. And I also want to thank all of you for your efforts and so on.

Now I have got a request and am looking for some help, and that is, at the present time we have had 6,000 requests that have come into our state health departments and our laboratories, and they are just overrun by requests and analysis of stuff that has been sent and so on. They're so overwhelmed that I am wondering how we might be able to use your associations to assist us in trying to reduce this number and also be able to help our other laboratories. I throw that out because it just came to my attention that the state labs are really stretched thin at this point and time, and I am trying to figure out a way how we might be able to buttress them and help them get the necessary resources they need. We may have to go in and get some extra money—I don't know, but I appreciate any comments.

I also would ask of your associations, please try and knock down this fear factor that is epidemic

across America. As professionals, you know that anthrax can be treated and treated very effectively by antibiotics. We have to somehow get the American public to understand that. I've been trying, but I need your medical professionalism to assist me to accomplish this.

So with that, I will now be more than happy to turn it over to Jeff Koplan for his remarks and then we will open it up for questions. Once again, before I do, I would just like to take this opportunity to thank the American Hospital Association and the American Medical Association for being such wonderful partners in this very perplexing and troublesome time in our country's history. Jeff?

Dr. Koplan:
Thank you, Mr. Secretary. I would like to thank everybody who is listening today. I know your days are extremely busy. You are pulled in every direction by clinical responsibilities, administrative responsibilities, the needs of patients in your communities—and the fact that you are taking a little time to sit with us today and learn a bit more about anthrax and share some of your concerns and questions with us we appreciate deeply.

A critical thing for us in public health is the linkage with clinical medicine. The bonds of that are true in every aspect of healthcare now, whether it is getting high immunization rates in a community, whether it is improving mammography screening, whether it is cutting down on tobacco use—nowhere is it more important than this area of bioterrorism. In over 50 years of CDC we have not had a real bioterrorism threat. We do now, and now is a good time for partnership. Now is a must time for partnership between you and us and getting the job done for the well being of the country.

We talk a lot about disease surveillance. Disease surveillance starts with you all. We play a part in it. Local, city, and county health departments, state health departments play a part in it. But really, the grassroots—that where the rubber meets the road in this is in you practicing clinicians' hospitals, folks in care in the community, emergency room doctors, infectious disease consultants, everybody. It's the surgeon who sees something for debrevement that looks unusual that needs to be thinking, "Could this be anthrax?" It's the pediatrician who is seeing a child with an unusual sore on their finger that looks like it might be a brown recluse spider bite, but thinks maybe it's something else. There is no community that is not potentially part of this. There is a tendency in popular culture to think that this can only happen in big urban settings, but we have seen already that that's not true. So wherever you are viewing from, wherever you are listening from, this is something that is germane, pertinent, and really important for both us and you to master some of this information. Many of us may have glossed over anthrax in medical school or in our postgraduate training. Well, we've learned in the last couple of weeks that we need to be experts in it, and the good news is, there is a pretty discrete body of knowledge to learn and we can all be experts in it in a pretty short period of time and you will be before this broadcast is over.

The role we would like you to play, and I think that you want to play just by virtue of having tuned in on this, is to be able to recognize some of these threats that are presented to us, recognize them quickly, and to play that role in linking what you do to what we do and in

stopping these outbreaks in their tracks. There is nothing more important in disease control than limiting the spread of disease. In this case anthrax does not spread person-to-person, but nevertheless, the earlier we detect an initial outbreak, the earlier we can apply control measures and limit other people from becoming ill from it. This link between public health and medicine is one we would like to further. A crucial part of this will be interplay between you in clinical practice and your local health departments and your state health departments. It was exemplary evidence in the Florida outbreak in which an astute clinician played a crucial role in getting appropriate laboratory samples to the state health department in an early diagnosis made of anthrax. I think there has been an underestimate of the quality of care provided in the U.S. and the astuteness of American clinicians, but this is something that this program and our activities here are in an attempt to even further, and to make sure that you are comfortable and confident of what you are doing when it comes to bioterrorist agents and anthrax in particular.

A couple of my colleagues here who are truly expert in this particular disease and its management and the public health aspects of it are going to be giving you considerable details promptly. I would also like to let you know that CDC is posting a variety of information, a variety of sources for health alerts, advisories, updates on a regular basis and it's appearing on our Emergency Preparedness and Response Web site, which is www.bt.cdc.gov. A fair amount of information is accessible there and will continue to be updated in the days and weeks to come.

Dr. Baker (moderator):
Great. Thank you very much, Jeff, and thank you, Secretary Thompson. We understand, Mr. Secretary, that your time is limited today, as is Dr. Koplan's, so we would like to get a couple of questions that have come in today right now from our viewers. We are only receiving questions by e-mail or by fax. We wondered if you, Mr. Secretary, would have time for one question?

Secretary Thompson:
Absolutely.

Dr. Baker (moderator):
One of the issues that has come in has to do with a question that you are asked very often, and that has to do with our state of preparedness in the country. You have been very supportive of the efforts that are now underway. Could you say a bit more about that issue, please?

Secretary Thompson:
Absolutely, and thank you for asking. First off, we have set aside this huge suite of offices right next to mine for actually planning and for dissemination and taking in of information 24 hours a day, 7 days a week. We also have a telephone line that you can call us for information. We have also hooked up CDC through our Health Alert Network with 37 states and we are in the process of getting the remaining 13 states hooked up. We have gotten 7,000 doctors and professional medical people (nurses and EMTs) that are on alert. They are distributed in 90 medical assistant teams and they can be moved relatively quickly. We have 8 strategically located push packages, each containing 50 tons of medical supplies and we are requesting from Congress an additional 200 tons of 4 more push packages located in other sites around America. We have 6,000 other doctors and medical people on the Commissioned Corps and professional people that could be

utilized by the Department of Health and Human Services to send out to a community or a state if they need it and we feel that we can respond. Our problem, of course, is that our state labs are really being overloaded now with all the fears by so many people asking for requests about a lot of stuff that really is not anthrax but people are fearful about it. I think that is about all I want to say at this point and time. I can go into greater detail if anybody wants.

Dr. Baker (moderator):
Great. Thank you. A question for Dr. Koplan: Jeff, the situation is changing from day to day. You are getting regular briefings and you are directly involved in the overall management of CDC's efforts around the epidemic. Could you update folks a bit on where we stand today?

Dr. Koplan:
Well, basically, we are dealing with focal outbreaks of disease. The initial one was in Florida and you will hear more details about that, but there we are dealing with 2 cases of disease, one other person with evidence of exposure of the disease, and a number of people are under antibiotic prophylaxis.

In New York, we have 3 cases of the disease, and again, focal exposures in certain workplaces and a number of people on antibiotic therapy. It is possible we will have a case or 2 more. They are under consideration and the laboratory work is being analyzed. But keep in mind, I think throughout this that it is a limited number of cases, a very limited number, a limited number of exposures that created a large amount of public and medical interest and certainly a huge amount of public health interest. We are deeply concerned and deeply involved in these, but the amount of morbidity and mortality—all of which is unfortunate and we wish we had none of it—remains circumscribed and indeed the need for action around these outbreaks remains relatively circumscribed. You'll hear more about the details of those from the participants here.

Dr. Baker (moderator):
Great. Thank you. Mr. Secretary, one last question for you if you have time for one last question.

Secretary Thompson:
Sure.

Dr. Baker (moderator):
As you know from a lot of the work that has gone on from both CDC and members of the Senate and the House, there is concern, as you mentioned earlier, about the state of the local public health infrastructure. You're now back in your state of Wisconsin as we understand. What are you feeling from communities around your state about local needs that exist either in your home state or in localities around the country?

Secretary Thompson:
Well, I'm just hearing that they are stretched, which we know they are and we want to be helpful. I think the fact that so many people are calling in with requests, and the laboratories are trying to handle them just because of the heightened awareness of everything that is taking place in America right now, that they are stretched pretty thin. What we are trying to do is to buttress

that with some additional appropriations through Congress in order to strengthen our local and state public health needs. We feel that even though it was terrifying and a terrible thing for America to go through on September 11, one of the good consequences of that, of course, is the fact that people now are aware of the need and the importance of putting more money into our local and state public health systems. That is why a good share of the 1.5 billion dollar request, outside of the medicine, is going to go for strengthening the local and state health departments.

Dr. Baker (moderator):
Mr. Secretary, we very much appreciate your support and also your willingness to take time with us today. We have one last question for Dr. Koplan and then we will go to a break. Jeff, could you say a little bit more about this issue of vigilance around the country? Practitioners like the ones in this program are clearly in a heightened state of vigilance. People are going to be perhaps needing to look for other unlikely things besides anthrax, and to look in places perhaps a little bit out of the way, not in our big cities—perhaps in rural areas. Could you say a little bit more about the need for increased vigilance, what people need to be looking for, and where does this vigilance need to apply?

Dr. Koplan:
I think—thanks—I think vigilance is a good way to put it. I guess I keep thinking back in my training, and probably most of you folks heard this in your training as well, is the old line for clinicians is, "When you hear hoof beats, think horses, not zebras." I think unfortunately what we need to do now is yes, still think horses, but in the back of your mind think, "Could there be a zebra in this pack that is going by?" That is where the vigilance comes in, and to think, "Is there anything unusual about this case that doesn't fit in with other ones? Have I seen a couple or 3 or 4 similar patterns in the last week or month that just don't fit the bill? Does it seem to be a clustering of something that might be unusual? Should I order that extra laboratory test, as unlikely as it might be?" A blood test, a culture, a patient that doesn't seem to be getting better on antibiotics that you would have thought would have been appropriate, etc., etc. You will hear more of the clinical details from my colleagues. But it is that vigilance that caused an infectious disease specialist in Palm Beach County to say, "Something doesn't fit in this patient; I'm going to ask for an anthrax culture and a smear." He might never have done it before, but something tipped this off, and that indeed is what gave us a big head start on coming to grips with this outbreak.

Dr. Baker (moderator):
Jeff, thank you very much. What we are going to do now is to take time, a brief video, and if you want to send us your e-mails or faxes, you've received the information. We want to thank Secretary Thompson and Dr. Koplan for being with us. They have other commitments and will be leaving the program at this point. We will be coming back with the second part of our program in just a moment. Thanks.

[Intermission]

Dr. Baker (moderator):
Welcome back. You have just heard about issues that relate to this broadcast in general terms.

But now we are going to turn to Dr. David Stephens, who is in the Meningitis and Special Pathogens branch here at CDC, and is a professor of medicine and director of the Division of Infectious Diseases at Emory University School of Medicine. David has clinical appointments at Emory University Hospital, the VA Medical Center, and Crawford Long Hospital, as well as Grady Memorial Hospital here in Atlanta. David, thank you for being with us today. David will talk to us today about clinical anthrax.

Dr. David Stephens:
Thank you very much, Ed. I think we have all learned a lot the last several weeks about anthrax. Let me present to you the basics. Anthrax is caused by the spore-forming bacterium *Bacillus anthracis*. It has historically been a zoonotic disease seen in sheep, goats, cattle, and follows the ingestion of spores in the soil. It is often seen now in developing countries. Anthrax has been rare in the United States. Infections are acquired through contact with anthrax-infected animals or animal products, or through (as in the case in Florida) intentional exposure. There are 3 clinical forms: cutaneous, inhalational, and gastrointestinal. This slide shows the etiology of anthrax, *Bacillus anthracis*. It is a gram-positive, spore-forming, nonmotile bacillus. It is seen on your left with the characteristic spores, and on your right, in a Gram stain of clinical material, the vegetative form of the organism is shown. Again, a gram-positive, spore-forming, nonmotile bacillus.

Anthrax comes in several clinical forms. First is the cutaneous form, which begins as a papule, progresses through a vesicular stage to a depressed black necrotic ulcer or eschar. Edema, redness and a necrosis without ulceration may occur. It's the form most commonly encountered in naturally occurring cases. These lesions are often painless. They may be pussy. They often develop in exposed sites on the hands, fingers and face.

The next form is inhalational anthrax. This is a clinical syndrome characterized by a brief prodrome resembling a viral-like illness occurring over a 2-3 day period, but sometimes longer. It is characterized by myalgias, fatigue, fever, with or without respiratory symptoms. This is followed by the development of hypoxia and dyspnea often with radiographic evidence of mediastinal widening. Meningitis occurs in 50% of patients. Inhalational anthrax has been extremely rare in the United States. There were only 20 or so reported cases in the last century.

The third form of anthrax is gastrointestinal anthrax. This is associated with abdominal distress, often followed by bloody vomiting or diarrhea and fever and signs of septicemia. It can present as oropharyngeal ulcerations with cervical adenopathy and fever. It develops after the ingestion of contaminated and poorly cooked meat.

This slide shows the virulence factors associated with *Bacillus anthracis*. Three important virulence factors are encoded by a plasmid, the pX01 plasmid, edema factor, protective antigen, and lethal factor. A second plasmid, pX02, encodes a capsule which inhibits phagocytosis.

The pathogenesis of anthrax is illustrated in this drawing. This illustration is by Drs. Dixon and colleagues and was published in the *New England Journal of Medicine* in 1999 and is a good source and good reference for information about anthrax. Spores may enter the skin, may enter

the gastrointestinal tract, may enter the pulmonary alveoli. They are taken up by macrophages. These spores vegetate into bacilli. Bacilli then are spread either by lymphatic spread or hematogenous spread to multiple sites. This organism through its toxins produces edema. It also produces a proinflammatory cytokine release characterized by the release of TNF Alpha and other cytokines leading to shock and ultimately, in some instances, to death. And as we mentioned earlier, meningitis is also a prominent feature of—may be a feature of inhalational anthrax.

Now I want to illustrate some of the manifestations of cutaneous anthrax. The vesicle may develop as early as Day 2. This progresses to a blackened eschar between Days 4-10 of cutaneous anthrax.

Again, another illustration of cutaneous anthrax from the Armed Forces Institute of Pathology's collection showing a vesicle on your left and ultimately the ulcer and eschar formation on your right.

This is also a series of pictures from the *New England Journal of Medicine* article I mentioned earlier showing cutaneous anthrax on the face and on the hand in different presentations. Again, for the purposes of recognition, this is another illustration of cutaneous anthrax to remind us—to remind you that this often occurs on exposed areas of the skin. The ulcer often has a heaped-up border or vesicular ring and progresses to this black eschar during its clinical course. Sometimes the lesions can be multiple, as seen here, with a considerable amount of edema.

Now let me turn to inhalational anthrax. This is due to inhalation of spores. It is felt that the number of spores required to produce inhalational anthrax (and this is supported by animal data) is between 8,000 and 40,000 spores. The incubation period is 2-3 days with a range of possibly up to 60 days. Spores are engulfed by macrophages and transported to mediastinal and peribronchial lymph nodes. The onset is insidious, with malaise, low-grade fever, non-productive cough. There is an abrupt development after this prodrome period of respiratory distress often accompanied by hemorrhagic mediastinitis. Bacilli are hematogenously spread, and as we mentioned earlier, in 50% of patients meningitis develops, which is often fatal.

This slide illustrates from an article in the *Journal of the American Medical Association* by Inglesby and D.A. Henderson, et al., looking at mediastinal widening associated with inhalational anthrax. This is a second illustration of a chest X-ray of mediastinal widening with pleural effusions.

Now, the differential diagnosis of cutaneous anthrax is long, as was mentioned earlier—spider bites or insect bites are often mentioned in the differential diagnosis. There are a number of other conditions, including ecthyma gangrenosum, ulceroglandular tularemia, plague, and even staphylococcal or streptococcal cellulitis.

Now, the differential diagnosis of inhalational anthrax is also long. It includes a variety of agents that cause pneumonia: *Mycoplasma*, *Legionella*, psittacosis, Q fever, viral pneumonias. Histoplasmosis with mediastinitis is sometimes mentioned in the differential diagnosis, as is

coccidioidomycosis. For patients who present with acute sepsis or acute meningitis, we should be thinking about anthrax in the differential as with down in the Florida case. There are a number of other causes of pneumonia which probably should be included in this list as shown.

Now the diagnosis of cutaneous anthrax is made by the characteristic eschar, in addition culture and Gram stain of vesicular fluid or exudates, blood cultures, biopsy. PCR is available, as is immunofluorescence and immunohistochemistry, which have been used in the diagnosis of the current cases.

Inhalational anthrax is associated with widened mediastinum, but not in all cases. Pleural effusions and blood or CSF cultures may be positive and Gram stains can be an important early clue. Again, PCR, immunofluorescence, and immunohistochemistry are important in establishing the diagnosis.

I have listed the current *MMWR* guidelines regarding postexposure prophylaxis to prevent inhalational anthrax. In adults these are ciprofloxacin or doxycycline, 500 mg po b.i.d. of ciprofloxacin, 100 mg po b.i.d. of doxycycline. The current recommended duration is 60 days. In children, again, the current recommendations are ciprofloxacin 10-15 mg/kg po q. 12 hours or doxycycline in the doses listed. I will comment that this dosing schedule is available on the CDC Web site.

I want to emphasize that cephalosporins should not be used in the treatment of *Bacillus anthracis* infection as *Bacillus anthracis* is resistant to cephalosporins. Additional recommendations concerning prophylaxis to prevent inhalational anthrax will be forthcoming as additional data is developed.

Now, the recommendations for initial anthrax treatment regarding inhalational or cutaneous exposure are listed on this slide. Again, they include ciprofloxacin or doxycycline; ciprofloxacin, 500 mg. po b.i.d. in adults, or doxycycline, 100 mg. po b.i.d. for 14 days. Inhalational anthrax is again intravenous ciprofloxacin or doxycycline. Ciprofloxacin and doxycycline are also currently recommended as initial therapy for children in appropriate doses. As more information becomes available on antimicrobial susceptibility these recommendations may be modified.

I want to end by emphasizing these points. I think it is very important that we do not panic. We must remain vigilant. Individuals must be—to develop anthrax—must be exposed to *B. anthracis* spores. To cause disease the spores must enter the skin, they must be swallowed, or they must be inhaled. Disease can be prevented after exposure to anthrax spores by early treatment with appropriate antibiotics. And lastly, anthrax is not spread from person to person.

Dr. Baker (moderator):
David, thank you very much for that very comprehensive and very useful discussion. What we would like to do now is to turn to our second expert, Dr. Brad Perkins. Brad, thank you for being with us today. Brad is with the Meningitis and Special Pathogens Branch here at CDC. He leads CDC's group of scientists with technical responsibility for anthrax. He is board certified in internal medicine and he is just back from Florida where he led the team that was investigating

the outbreak there. Good to have you with us.

Dr. Brad Perkins:
Thanks very much. It is a pleasure to have an opportunity to talk with all of you about medicine and public health and give you an inside glimpse at some of the strategies we are using to investigate these outbreaks and to help us define the cases and the approaches we are going to recommend to identify people that are at risk and get them on appropriate therapy.

On October 4, through the efforts of an astute physician, as Dr. Koplan has already mentioned, we were notified of a suspected case of inhalational anthrax. By the next morning, even before the case was confirmed at CDC and state public health laboratories, we had teams ready and on route to 2 locations that the case patient (or the index patient) had visited within the incubation period for inhalational anthrax, Florida and North Carolina. This slide outlines the investigative strategy. Early in the investigation the 2 primary focus areas were the case investigation (that's the *who*, *what*, *when* and *how* did this individual contract inhalational anthrax) and surveillance. Both of those efforts proceeded intensively in parallel in both Florida and North Carolina. As those investigations proceeded, intervention strategies were designed based on the information that was yielded from those efforts. For example, in the case investigation, we rapidly ascertained that there was no clear explanation for natural exposure that could account for the inhalational anthrax case. In addition, through our surveillance efforts we found that there was a second case of inhalational anthrax also employed by the same company as the index patient. Through selected and epidemiologically driven environmental sampling of the index patient's place of employment we identified contamination with *Bacillus anthracis* in multiple locations of the building. Those pieces of combined information that were yielded from case investigation and surveillance allowed us to design an intervention strategy that included targeting approximately 1,000 persons that we felt may be at risk for inhalational anthrax. That intervention was delivered, those people are on antibiotics, and we have identified no further cases of inhalational disease. Still, there is an ongoing public health and criminal investigation to try to completely define the circumstances of this exposure.

Let me tell you a little bit about anthrax case definitions. These are epidemiologic case definitions that have some relevance to clinical medicine, but are primarily designed to help us track the occurrence of these cases on local, state, and national levels. We are considering a confirmed case of anthrax to be a person that has a clinically compatible illness with isolation of *Bacillus anthracis* from affected sites or tissues, or two supporting non-culture laboratory tests. Those nonculture tests may include staining with immunohistochemical staining techniques, PCR studies identifying DNA of *Bacillus anthracis* in clinical tissues or from clinical sites, or serology that suggests that there has been seroconversion or strong seropositivity to the anthrax organism.

For a suspected case, we are considering that there needs to be a clinically compatible illness, and in this situation we don't have isolation of *Bacillus anthracis*, but we have at least one supportive non-culture laboratory test, or we have an epidemiologic link to a confirmed environmental exposure. That is, we know this person was exposed to a letter in which *Bacillus anthracis* has been identified or to some other source of environmental contamination that has

been documented.

I want to go over just briefly what we would suggest is an algorithm for action for clinicians when encountered or when there is a suspected anthrax case. These steps—these three steps—must be entertained simultaneously. First of all, if there is any suspicion of anthrax, the patient has to undergo appropriate clinical testing. Beyond the clinical suspicion, the tests that can serve as early confirmatory evidence of anthrax include Gram stain of affected tissues or sites, culture (we are in very good shape with culture because this organism grows extremely well on traditional culture media that's available in all clinical laboratories), or biopsy of affected sites, particularly in the case of cutaneous anthrax.

The treatment of the patient when anthrax is suspected should be based on the clinical impressions of the physician. It is unlikely that there will be definitive test results from any of these methods so that treatment—initial treatment, as Dr. Stephens has outlined—should be begun on clinical suspicion. While all of this is going on, just as the physician in Palm Beach County did, you must notify local or state public health authorities. That is going to trigger the larger investigation, the larger public health response that is necessary for rapid identification of persons that may be at risk for developmental, inhalational, or other forms of anthrax.

Right now we are experiencing and actively engaged in a number of investigations that are presenting a variety of challenges to the public health system. In Florida, we were presented with inhalational cases first, with no obvious vehicle. In New York City, we were presented with cutaneous disease with a confirmed vehicle, a letter that was positive for *Bacillus anthracis*. And lastly, most recently in Washington, D.C., we are presented with a situation where there is no obvious disease, but a very recent exposure with a confirmed vehicle or letter. This set of experiences is serving as a basis for us to develop a public health framework to approach these situations in a systematic and scientifically based manner.

So in closing, I would like to suggest that the clinicians are our first line of defense for bioterrorism in the United States. We want you to be suspicious at this time. We want you to consider testing for *Bacillus anthracis*, and as those situations arise, report to your local and state public health authorities so we can get into the public health investigation and identify people that may be at risk for development of disease. Thank you.

Dr. Baker (moderator):
Brad, thank you very much. We'd like to share a little bit more information with you about the issue of reporting. You have just heard about clinical and epidemiological issues related to anthrax. I would like to give you a brief overview of how our nation's public health agencies operate and then how you as clinicians should relate to them. Each of you is served by both a local and a state governmental public health agency. In some states, the state health department is also responsible for governmental presence at the local level. To help you identify the points of contact for your location, CDC, in partnership with our local and state public health colleagues, has developed a new health department locator system, which can be accessed via the Web at www.phppo.cdc.gov, and by entering your location you will then be directed to the appropriate health official. This resource, we believe, will be especially important as you report

suspect cases of anthrax or request information regarding management of specific situations. CDC will also be providing you with alerts and updates through our Health Alert Network, which goes out to over 2,300 hospitals around the country. At the end of this broadcast we will provide information to you on how to link to that network system.

CDC also publishes the *Morbidity and Mortality Weekly Report*. I would like to show you the copy that is now accessible over our Web site. As you know, this journal publishes—the *Journal of the American Medical Association* reprints the *MMWR* to facilitate distribution to you. This week's issue features 2 important articles: one, a summary of the investigation that Dr. Perkins just described, and secondly, an article on recognition of illness that really relates to the issue of heightened surveillance. Both of these articles are available now at our main Web site, www.cdc.gov.

CDC is also building partnerships with academic institutions for the creation of a national network of CDC Centers for Public Health Preparedness to provide regional and national training information and consultation resources for public health practitioners addressing these challenging problems. We will continue to provide advice through our distance learning courses such as today's broadcast through the Public Health Training Network, and laboratory training through the National Laboratory Training Network. For further information, again, our Web site has it available to you.

Finally we want to direct your attention to the part of the CDC Web site which has, as you might imagine, received very heavy traffic in recent days. In fact, Dr. Koplan mentioned it earlier. Today there were over a million hits on this part of the Web site, and the address, as he gave you earlier, is www.bt.cdc.gov. This site includes a wide range of clinical and public guidance which is being updated on a daily basis with authoritative and scientifically accurate information.

Now let's turn to your questions. As you might imagine, we will not be able to respond to every question today, but we will do our absolute best to use your questions as a guide in updating our Web site and other information resources. We are considering additional videoconferences of this type and your questions will help us to plan for the future.

For our first question I'd like to turn to Dr. Perkins. You described the Florida investigation for us very well. The question has come in, is in doing that Florida investigation, when did you and your team first suspect that the 2 cases of inhalation anthrax might have been related to an intentional release of the bacteria?

Dr. Perkins:
Thank you, Ed. That's a good question. I think we need to put the beginning of the investigation in appropriate context. For the last several years we've dealt with a very large number of hoax incidents. Generally, they've involved letters or packages usually containing a powder and frequently labeled as being anthrax. Up until the time we began the Florida investigation we had never identified a letter or a package that actually contained *Bacillus anthracis*. Even so, that has changed of course, with the incidents in New York City and Washington D.C. that occurred after the beginning of the Florida investigation. Even so, we approached the Florida single case of

inhalational anthrax with an open mind as to whether this could be a naturally occurring case or whether it was the result of intentional exposure. Of course, we had heightened suspicion. This was the first case of reported inhalational anthrax in the United States in more than 25 years. There was the temporal association with the events of 9/11, and we knew going into the investigation that initial interviews conducted by the local and state health departments had revealed no obvious source for environmental or natural exposure for inhalational disease. When we found *Bacillus anthracis* spores in the index patient's work place, and then identified a second case of inhalational disease in an employee of the same company who worked in the mailroom, we were quite suspicious. What clenched our suspicion, however, was the directed environmental sampling we did in the work place which revealed multiple sites of contamination, the index patient's keyboard, and the mailroom, and at that point the investigation became both a combined public health and a criminal investigation.

Dr. Baker (moderator):
Great. Thank you very much. One of the issues that you faced in Florida, and both of you have referred to this previously, has to do with the use of antibiotics in these particular situations. It would be I think very helpful to know what the decision-making process was that you went through in deciding who should be given postexposure antibiotic prophylaxis for prevention of inhalation anthrax in Florida. How did you approach that?

Dr. Perkins:
Well, for the last several years we have worked at CDC and with many of our partners to develop recommendations for postexposure antibiotic prophylaxis. David Stephens has summarized those guidelines and they are also included in today's *MMWR* or CDC's weekly public health report.

Our decisions about who needs antibiotics in these situations are driven primarily by intensive epidemiologic investigations. The purpose of these investigations is to thoroughly describe the circumstances in which suspected exposures or confirmed exposures may have taken place. Those investigations are designed so we can identify everyone that is at risk. As an adjunct to these investigations we are using a number of laboratory tools to help us better define populations that may benefit from antibiotic therapy. Some of the laboratory tools that we have used have included nasal swabs for identification of *Bacillus anthracis* in the nose. We have also used very targeted environmental sampling in environments we think may be contaminated with anthrax spores, and in some circumstances we've actually obtained serology to look for persons that may have been exposed to anthrax.

I think that it is important to note that all of these laboratory strategies—laboratory-based strategies—are really an adjunct to the epidemiologic investigation. There has been some confusion about the use of these tests in this situation and none of these—none of these laboratory-driven techniques are designed to be used in individual patient management decisions. All of them are designed to support the epidemiologic investigation and to be used in combination with it to identify populations that would benefit from antibiotic therapy.

Dr. Baker (moderator):

So it's not a simple decision, you have to integrate a lot of information together to decide about when to start somebody on prophylaxis?

Dr. Perkins:
Exactly. One of the things that we are finding is that some number of people may be initially started on antibiotics, but as we get more information to help us clarify the circumstances of exposure more carefully, we may actually revise those recommendations, hopefully target a smaller group of people before we commit them to this long-term (but we think very important) course of antibiotic therapy.

Dr. Baker (moderator):
There is a question I think about antibiotic availability. People are certainly aware of the fact that the folks that purchased antibiotics, there are some people that are keeping them in their houses and so forth. But the question really for Florida has to do with what really happened? How are these antibiotics that were given to individuals, where did they come from, how are they supplied in that particular situation?

Dr. Perkins:
Yes, in the Florida situation, as soon as we decided that we needed to treat a targeted group of individuals who were at risk for inhalational disease, we contacted the CDC National Pharmaceutical Stockpile personnel and they mobilized to deliver oral antibiotics and the personnel that were needed to logistically support the delivery of those antibiotics in a very short period of time. Actually, we decided to treat individuals on Sunday evening, October 5, at about 7:00 in the evening. We decided that about 1,000 people could benefit from treatment with antibiotics. We mobilized the National Pharmaceutical Stockpile at that time. At 5:30 the next morning, all of the equipment that was needed to deliver those antibiotics and personnel to support the delivery of those antibiotics were on the ground in Palm Beach County and at the clinic ready to go to work passing out these antibiotics at 9:00 the next morning. So the system worked beautifully. You know, I'm sorry we had to use it, but it worked very well.

Dr. Baker (moderator):
So what you are saying is, it took about 10 hours, a little more than 10 hours, from the time you decided you needed the medicine to having it be on the ground with the people, ready to deliver it in Palm Beach, Florida?

Dr. Perkins:
Yes, and it actually could have happened faster. That timing was designed with the thought in mind that we could not get people in to get the antibiotics before about 9:00 in the morning. So the Stockpile actually has the ability in this circumstance to even deliver earlier than that.

Dr. Baker (moderator):
Right. And as you know, the Stockpile has also been deployed to other sites around the country in very short periods of time just as with the case there.

Dr. Perkins:

Exactly.

Dr. Baker (moderator):
Another question that's come in has to do with this drug called "cipro," which seems to now be almost a household word. David, could you say a little bit more about some of the side effects here of ciprofloxacin?

Dr. Stephens:
Sure, Ed. Ciprofloxacin is a fluoroquinolone antibiotic. It has been used for a number of years. It does have some side effects, but they are relatively minor in terms of their—usually minor. These side effects include gastrointestinal complications, which is diarrhea and vomiting. In about 1% of patients there may be some increased CNS irritability, but in general ciprofloxacin is a safe and effective antibiotic and has been used for some time.

Dr. Baker (moderator):
What about other drugs? In your earlier presentation you mentioned doxycycline as a drug that has also been thought about, and there are other drugs that are out there that have been mentioned in this context. Could you say a little bit more about the risk of using tetracyclines and also fluoroquinolones, particularly in children, and say a little bit more about whether these alternatives are really available to us, David?

Dr. Stephens:
I think this is an obvious concern and in—there are some potential complications of ciprofloxacin and doxycycline in children. Those include issues in very young children with dental enamel (with tetracyclines). They also include issues of potential cartilage—interference with ligament and cartilage formation in children receiving ciprofloxacin. However, this must be taken into account in the context of a life-threatening situation such as inhalational anthrax, and those risks must be weighed. It is also important that additional antimicrobial susceptibilities be determined in all new isolates to help us determine other alternative regiments for both prophylaxis and treatment in children.

Dr. Baker (moderator):
Great. Thank you very much. Brad, let's turn back to this case definition if we could for a minute. This is a real important part of our program today because obviously our desire is to have clinicians out there report to their local or state health department if a case occurs. So maybe we can go over that again.

In the anthrax case definition you mentioned that culture or other laboratory tests that could be used to confirm an anthrax case. Could you tell us then some more about how clinicians can get this testing on a suspect case? How is that available?

Dr. Perkins:
Well, again, I think this is a very important area. The case definitions I presented earlier are designed to reflect various levels of diagnostic certainty in patients with clinically consistent illness either with or without known exposure to *Bacillus anthracis*. We would like to see culture

isolation from all of these because we feel that that's the gold standard for diagnosis, but that is not possible in all circumstances and we are fortunate to have a variety of other laboratory tools that will allow us to confirm cases of disease. In the routine clinical setting it is possible to get a fair ways down the road in terms of diagnosis of anthrax disease in just the regular clinical microbiology laboratory. Again, this organism grows phenomenally well on routine sheep blood agar plates that are used in essentially all clinical laboratories. It is easy to get the bacillus level identification, and at that level any bacillus species that is nonmotile, nonhemolytic that is growing under aerobic conditions should be quite suspicious in a setting of clinically consistent illness. And actually even that level of diagnostic confirmation should trigger a report to the public health system.

What's difficult is when you get beyond that. It is actually quite challenging to distinguish many of the other bacillus species from *Bacillus anthracis*. At that point we have established—CDC has established a network of laboratories. The Laboratory Response Network for bioterrorism, which is a public health—part of the public health infrastructure to move these specimens or strains related to these high threat agents such as *Bacillus anthracis* into a setting where further confirmatory testing can be done. And so if someone has a bacillus species in their clinical laboratory they need to contact their local and state public health authorities and work with them to get that isolate into the Laboratory Response Network for bioterrorism. These laboratories are all connected to CDC. They are using standard protocols and reagents that have been provided by CDC and other partners in bioterrorism, and they have the ability to confirm, in almost all instances, an identification of *Bacillus anthracis*.

Now when we don't have culture, when we don't have an isolate, there are some other tests. These tests are less available in clinical laboratories and actually in some of the Laboratory Response Network as well. They can be used to confirm cases, but they are generally less available and some of them you actually have to come into CDC laboratories to get those tests. That's the PCR test for detection of *Bacillus anthracis* DNA; the immunohistochemistry test, which uses antibodies that allow us to visualize *Bacillus anthracis*; and then the serology test, which is a research test that currently is only available at CDC.

Dr. Baker (moderator):
What you described sounded to me like sort of a 3 level system. In local hospitals, in local communities, the capacity is there to basically identify the organism, and that would lead the clinician in to make a report to the health department. That's kind of that first level—is that right?

Dr. Perkins:
Exactly. After the bacillus species in the setting of clinically suspicious illness.

Dr. Baker (moderator):
And that would trigger that case report that you talked about earlier?

Dr. Perkins:
It should trigger that case report and that's exactly what happened in the Florida situation.

Dr. Baker (moderator):
And the second level is more the Lab Network, that's the more definitive identification. The third level are those very specialized tests that you mentioned at the end.

Dr. Perkins:
Yes.

Dr. Baker (moderator):
So it's sort of a 3-tiered system.

Dr. Perkins:
That's exactly right.

Dr. Baker (moderator):
Let's go on to some other issues here. The question has come in regarding anthrax vaccine, whether or not it is available, whether or not it is the thing that should be done here in this setting. Could one of you help us with the issue of anthrax vaccine?

Dr. Stephens:
Sure. We both may want to comment. There is an anthrax vaccine; it was developed through the efforts of the Centers for Disease Control some years ago in prevention of disease when workers exposed to wool and goat hair became ill with wool sorter's disease in the '50s and '60s when inhalational anthrax was a problem. The vaccine is currently not recommended except for those individuals who work with *Bacillus anthracis*. And, Brad, you may want to comment on that issue.

Dr. Perkins:
Yeah, the people that have generally been vaccinated with the anthrax vaccine in this country are those people that have an occupational risk for exposure. At this time, the vaccine is only used in those individuals as well as the military population, although we are actively vigilant for situations where it may be beneficial to use the vaccine in the civilian population.

Dr. Baker (moderator):
So basically what you are saying is, the general population does not need to even think about anthrax vaccine. That is not an issue. It is really related to those individuals that have a very clear risk of anthrax as a result of doing certain occupational things like the wool sorters and the things that you mentioned before.

Dr. Perkins:
Exactly.

Dr. Baker (moderator):
Now there are other people out there that in their work are concerned about being exposed to anthrax—for example, first responders, healthcare providers and those kinds of individuals, who,

again, across the country, would have a very low likelihood of being in contact with anthrax. But again, people are starting to wonder, "Is this something I need to be thinking about in my occupation?" Obviously, not the traditional things that you talked about. Are we developing guidelines that go beyond those traditional occupations to think about other groups?

Dr. Perkins:
Well, the Advisory Committee for Immunization Practices, which is CDC's recommendation for use of licensed vaccines, entertained this issue in quite a substantive way over the last couple of years. There was a statement made by that committee that suggests that there is no current need for any pre-exposure vaccination of specific populations in the United States. Populations that were considered included emergency first responders, law enforcement officials, persons that would receive suspicious packages in the laboratory. At that time there was a firm recommendation from the committee that there was no need for pre-exposure vaccination because there was no ability at that point to calculate risk versus benefit of that protection. Over the last month we are seeing the occurrence of cases and the occurrence of risk and I think that based on that change of risk that we are going to have to re-evaluate the need for vaccination in selected populations.

Dr. Baker (moderator):
So we are rethinking that question in light of recent events basically?

Dr. Perkins:
We are. We are.

Dr. Baker (moderator):
A different question on nasal swabs. We've heard about nasal swabs. You did a lot of nasal swabs in Florida, and that is happening now in various places around the country. Maybe, David, you can help us with this. What can you say about when it is indicated and what do nasal swabs really mean? What is the significance of that?

Dr. Stephens:
Nasal swabs, as Brad has indicated, were used and are being used in settings of epidemiological investigations regarding these anthrax outbreaks. However, they shouldn't be used in an individual situation for making decisions. And I think that Brad would agree with that. The key element is that they serve a purpose in epidemiological investigation studies, but not for the individual decision-making regarding prophylaxis or treatment.

Dr. Baker (moderator):
Would you say it is fair to say that a nasal—a positive nasal swab is really more a measure of exposure? It means that person has been around the bacillus but it doesn't have direct clinical implications in terms of triggering, say, drug use. Is that a correct statement?

Dr. Perkins:
That is exactly correct. Again, the decisions about antibiotic prophylaxis are driven by the epidemiologic investigation, and the nasal swabs, the environmental sampling, and the potential

serology done are all adjuncts to the epidemiologic investigation, trying to draw circles around populations that are at risk. Those tests—none of those tests should be used to make individual decisions about this patient or this individual should be treated and this one should not.

Dr. Baker (moderator):
Let's turn a little bit to sort of the early part of the action. You talked about this a little bit in your description of Florida. That's this issue of a suspicious letter or a package. Many people now want to know what they should do. How does one identify a suspicious package? What are we now learning about how to handle these letters or packages from the ongoing investigations?

Dr. Perkins:
We are learning some interesting things. We are learning some things about human nature. We have literally—in the context of the multiple investigations that CDC is currently involved with—we literally interviewed hundreds of people that have been involved in handling or exposure to either confirmed or suspected envelopes or packages containing *Bacillus anthracis*. There are a couple of things that have emerged from that experience. First of all, when someone opens or finds a suspicious envelope or package that contains powder, we would strongly recommend that they do not carry the letter around an office environment, for example, and show it to people. We are finding that that's quite a frequent response to finding something unusual or something that people don't understand.

Secondly, we are finding that people often, when they get a powder or a substance and they don't know what it is, they will do two things: they will try to smell it to determine what it is or they will try to look at it very closely. Both of those things are extremely dangerous practices if the material actually contains *Bacillus anthracis* spores.

Lastly, some recommendations have suggested that if a suspicious envelope or package is identified, that a plastic bag or a container should be identified and that the suspicious letter, or envelope, or package should be put inside that container. As we start to understand more about these exposures I would suggest that's probably not what we want people to do. I think the most prudent advice at this point is that if something suspicious is received, that it is carefully laid down on the nearest flat surface, that it is left there, that the person and anybody else in that room leave the room and call 911 for assistance.

Dr. Baker (moderator):
Any further thoughts on that, David?

Dr. Stephens:
I certainly think that suspicion for anthrax and notifying your state health department and following the instructions that Brad just gave you is sound advice.

Dr. Baker (moderator):
Great. I want to thank both of you for being with us today and also for all that you are doing on this extraordinary situation here at CDC. Thank you for being with us today.

Drs. Perkins and Stephens:
Thank you.

Dr. Baker (moderator):
That brings our program really to a close. I want to say that at the completion of this broadcast, this program will be available online at the Web site address that is on your screen: www.cdc.gov/phtn. For further information on the Health Alert Network that was mentioned before, there is a different Web address, and that's on your screen as well. We also plan to rebroadcast this program on Monday, October 22, from 5:00 until 6:30 p.m. Eastern Daylight Time. At that point, please check satellite coordinates; they will be different from those today. Additionally, you may obtain a VHS tape of this program free of charge from the Public Health Foundation by calling 1-877-252-1200 between 9:00 and 5:00 Eastern Standard Time. International callers should call 301-645-7773. Thank you very much for joining us and we also want to again express our appreciation to our three experts for providing us with this exceptionally informative program. Thanks very much to Secretary Thompson and particularly thanks to our partners at the American Medical Association and the American Hospital Association. Thank you very much for being with us today.