

**CENTERS FOR DISEASE CONTROL AND PREVENTION**

**ANTHRAX: WHAT EVERY CLINICIAN SHOULD KNOW**

**OCTOBER 18, 2001**

**ATLANTA, GA**

**DR. ED BAKER:** 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 health care providers, and many other colleagues working in a variety of settings in 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 exposure.

As you have read in the program fact sheet, the goal of this program is to provide physicians, nurse clinicians and other health care 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 suspect anthrax exposure.

And to accomplish this, we have three 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's 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 in the community.

Before I introduce the faculty, I'd like to take care of a few administrative issues. If you're having technical problems, call 1-800-728-8232. From outside the United States, the number is 404-639-1289.

If you're viewing the broadcast through a subscription network and experiencing technical difficulties, please contact your network's technical assistance line.

Today, we'll not be taking any live calls but if you're interested in asking questions, you may fax them or email them to us. The fax number is 800-553-6323. If you cannot use the toll free 800 number, or are watching us outside of the United States, our fax number is 404-639-0181.

Our email address is [phtnlive@cdc.gov](mailto:phtnlive@cdc.gov). We also have a TTY number. It's 800-815-8152. If you cannot use our 800 number and are watching outside the US, the TTY number there is 404-639-0182. Please note, we encourage you to videotape this broadcast.

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 for 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'd 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 and the Public Health Training Network.

And I'd also like to thank the many public private subscriber military networks that are assisting us in making this program available across the nation. Thanks to all of you and now we'd like to hear from Secretary Thompson.

**SECRETARY TOMMY THOMPSON:** Hello. Who's on?

**DR. BAKER:** Secretary Thompson. This is Dr. Ed Baker at CDC with Dr. Koplan and Dr. Stephens and Dr. Perkins.

**SECRETARY THOMPSON:** Wonderful.

**DR. BAKER:** And you are broadcasting live to our network.

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

**DR. JEFFREY P. KOPLAN:** Absolutely.

**SECRETARY THOMPSON:** Okay. Are the doctors and the hospital associations both on the line?

**DR. BAKER:** 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's issued a wonderful call to action in which he's 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's exactly the right tact 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 are on this teleconference call this afternoon, and I appreciate and thank you for taking your time out to hear from CDC and myself as Secretary. I believe your both organizations 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. And we're working vigorously with our federal partners to coordinate domestic preparedness, and I believe we're 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 bio-terrorism preparedness efforts into my immediate office upon being selected as Secretary of Health and Human Services, and I appointed Dr. Scott Lillibridge of the Centers for Disease Control, and one of the nation's leading experts on bio-terrorism, to head the Office for National Security and Bio-Terrorism.

His office is on my floor in the HHS Building, right across from my office. And 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, seven days a week, in a conference room a few steps from my office to coordinate the intel that's 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, which is going to be headed by Dr. D.A. Henderson, and all of you know he's the physician who lead the successful fight to eradicate small pox, and he's on board almost on a daily basis.

The President has now requested an additional \$1.5 billion to combat terrorism to strengthen our ability to prevent and respond to a bio-terrorism attack and the request is, of course, is more than a six-fold 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 to speed the development and purchase of 300 million dosage of small pox vaccine.

We're going to also add four more push-packs to the current eight. 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 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 has been likely under--been largely under-funded for several years.

I also believe, and I've asked Congress--this is my request, it's not the President's. It's 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 health state department and every regional office.

We're also putting an additional \$50 million in to strengthen our metropolitan medical response system, and it will go from 97 communities to 122.

These are 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, that of CDC, led by Jeff Koplan.

And I would like to just add that I think CDC has just done an exemplary fine job throughout this whole thing, and I can't tell you how much I appreciate their support and partnership and the professionalism by which they've conducted their work. And I also want to thank all of you for your efforts and so on.

Now I've got a request and looking for some help and that is, at present time, we've had 6,000 requests that have come into our state health departments and our laboratories, and they're just overrun by requests and analysis of stuff that has been sent and so on. They're so overwhelmed that I'm 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 out in the laboratories.

And I throw that out because it just came to my attention that the state labs are really stretched thin at this point in time, and I'm 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 or I don't know, but I appreciate any comments. And I also would ask of your associations please try and knock down this fear factor that's epidemic across America.

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

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

**DR. KOPLAN:** Thank you, Mr. Secretary. I'd like to thank everybody who's listening today. I know your days are extremely busy. You're pulled in every direction by clinical responsibilities, administrative responsibilities and the needs of patients in your communities, and the fact that you're taking a little time to sit with us today and learn a little 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. And the bonds of that are true in every aspect of health care now, whether it's getting high immunization rates in the community, whether it's improving mammography screening, whether it's cutting down on tobacco use.

Nowhere is it more important than this area of bio-terrorism and, in over 50 years of CDC, we have not had a real bio-terrorism threat and we do now, and now is a good time for partnership. Now is a must time for partnership between you and us in getting a 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 and city and county health departments, state health departments play a part in it.

But really the grass roots, the 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 debrievement (sp) that looks unusual and that needs to be thinking could this be anthrax.

It's the pediatrician who's seeing a child with an unusual sore on their finger that looks like it might be a brown recluse spider bite but thinks, but maybe it's something else.

There's no community that's not potentially part of this. There's a tendency in popular culture to think that this can only happen in big urban centers, but we've seen already that that's not true.

So wherever you're viewing from, wherever you're 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's a pretty discreet 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 presenting to us, recognize them quickly, and to play that role in linking what you do to what we do and then stopping these outbreaks in their tracks.

There's 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, and a crucial part of this would be interplay between you and clinical practice and your local health departments and your state health departments. It was in exemplary evidence in the Florida outbreak, in which an astute clinician played a crucial role in getting appropriate laboratory samples to state health department, and an early diagnosis made of anthrax.

And I think it--there has been an underestimate of the quality of care provided in the US and the astuteness of American clinicians, but this is something this program and our activities here are an attempt to even further, and make sure you're comfortable and confident of what you're doing when it comes to bio-terrorist 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. But I'd also like to let you know that CDC's posting a variety of information, a variety of sources, health alerts, advisories, updates on a regular basis, and it's appearing on our emergency preparedness and response Website, which is [www.bt.cdc.gov](http://www.bt.cdc.gov). And a fair amount of information is accessible there and will continue to be updated in the days and weeks to come.

**DR. BAKER:** 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'd like to take a couple of questions that have come in today right now from our viewers. We're only receiving questions by email or by fax and we wondered if you, Mr. Secretary, would have time for one question.

**SECRETARY THOMPSON:** Absolutely.

**DR. BAKER:** One of the issues that's come in has to do with the question that you're asked very often, and that has to do with our state of preparedness in the country. You've 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 on a 24 hours a day, seven days a week. So we also have a telephone line that she comes in there and she can call us for information.

We have also hooked up CDC through our health action alert network with 37 states and we are in the process of getting the remaining 13 states hooked up.

We have got 7,000 doctors and professional medical people, nurses and EMTs, that are on alert and they are distributed in 90 medical assistant teams. And they can be moved relatively quickly.

We have eight strategically located push-packages, each containing, excuse me, each containing 50 tons of medical supplies, and we're requesting from Congress an additional 200 tons or four more push-packages located in other sites around America.

And we have 6,000 other doctors and medical people in the commission core and professional people that could be utilized by the Department of Health and Human Services, to send out to a community or to 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 varied request about a lot of stuff that really is not anthrax, but people are fearful about it.

I think that's about all I want to say at this point in time. I can go into greater detail if anybody wants.

**DR. BAKER:** Great. Thank you. A question for Dr. Koplan. Jeff, the situation is changing from day to day and you're getting regular briefings and you're 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're dealing with focal outbreaks of disease. The initial one was in Florida, and you'll hear more details about that, but there, we are dealing with two cases of disease.

One other person was evidence of exposure to the disease and a number of people are under antibiotic prophylaxis.

In New York, we have three cases of disease and again, focal exposures in certain work places and a number of people on antibiotic therapy, and it's possible we will have a case or two more. They're under consideration and laboratory works 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. They've 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 would wish we had none of it, remains circumscribed and, indeed, the need for action around these outbreaks remains relatively circumscribe.

And you'll hear more about the details of those from the participants here.

**DR. BAKER:** Great. Thank you. Mr. Secretary, one last question for you if you have time for one last question.

**SECRETARY THOMPSON:** Sure.

**DR. BAKER:** As you know, from a lot of the work that's gone on from both CDC and members of the Senate and the House, there's 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 it. What are you hearing 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. And I think the fact that so many people are calling in with requests and the laboratories are trying to handle them, just because the heightened awareness of everything that's taking place in America right now, that they're stretched pretty thin.

And what we're trying to do is to buttress that with some additional appropriations through Congress in order to strengthen our local and state public health needs. And 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. And that's why a good share of the \$1.5 billion request outside of the medicine is going to go for strengthening the local and state health departments.

**DR. BAKER:** Well, 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'll go to a break. Jeff, could you say a little bit more about this issue of vigilance. Around the country, practitioners like the ones on this program, are clearly at a heightened state of vigilance and 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--Ed, thanks--I think vigilance is a good way to put it, and I guess I keep thinking back and our training, and probably most of you folks out there heard this in training as well, is, you know, the old line for clinicians is when you hear hoof beats think horses, not zebras.

And 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's going by.

And that's 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 three or four similar patterns in the last week or month that just doesn't fit the bill? It would 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. And you'll hear more of the clinical details from my colleagues. But it's 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.

And might never have done it before, but something tipped us off and that indeed is what gave us a big head start on coming to grips with this outbreak.

**DR. BAKER:** Great. Jeff, thank you very much. What we're going to do now is to take time, a brief video, and if you want to send us your emails 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'll be coming back for the second part of our program in just a moment. Thanks.

Welcome back. You have just heard about issues that relate to this broadcast in general terms, but now we're going to turn to Dr. David Stephens, who is in the meningitis and special pathogens branch here at CDC, and is also 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've all learned a lot in the last several weeks about anthrax.

Let me present to you the basics. Anthrax is caused by the spore forming bacterium, bacillus anthracis. It is historically been a zoonotic disease seen in sheep, goats, cattle, and follows the ingestion of spores in the soil. It's often seen now in developing countries. This 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 of Florida, intentional exposure. There are three clinical forms: Cutaneous, Inhalational and Gastrointestinal.

This slide shows the etiology of anthrax, bacillus anthracis. It is a gram positive spore forming non-motile bacilli--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 non-motile 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/or necrosis without ulceration may occur. It's the form most commonly encountered in naturally occurring cases. These lesions are often painless. They may be pruritic. 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 two to three day period, but sometimes longer. Characterized by myalgias, fatigue, fever with or without respiratory symptoms.

If this is followed by the development of hypoxia and dyspnea, often with a radiographic evidence of mediastinal widening.

Meningitis occurs in 50 percent of patients. This condition has, or this infection or this form of anthrax, has been extremely rare in the United States. There are 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 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 is by a Drs. Dixon and colleagues, and was published in the New England Journal of Medicine in 1999, and is a good source and a good reference source for information about anthrax.

Spores may enter the skin, may enter the gastrointestinal track, 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 hemotogenous (sp) spread to multiple sites.

This organism, through its toxins, produces edema as we've illustrated. It also produces a pro-inflammatory sidaan (sp) release, characterized by the release of TNF alpha and other sidaan 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. Vesicle may develop as early as day two. This progresses to a blackened eschar between days four to ten of cutaneous anthrax.

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

This is the also 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, another illustration of cutaneous anthrax to remind us, similarly to remind you, that it occurs on exposed areas of the skin.

The ulcer often has a heat border, a 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, which may be associated with cutaneous anthrax.

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 two to three days, with a range of possibly up 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 abrupt development after this prodrome period of respiratory distress, often accompanied by hemorrhagic mediastinitis, hemotogenous spread and, as we mentioned earlier, in 50 percent of patients, meningitis, which is often fatal.

This slide illustrates from a article in the Journal of American Medical Association by Englesby, et al., and D.A. Henderson looking at mediastinal widening associated with inhalational anthrax.

This is the second illustration of mediastinal widening and pleural effusions on chest x-rays in seating an inhalational anthrax.

Now, the differential diagnosis of cutaneous anthrax is long. As we mentioned earlier, spider bites or insect bites are often mentioned in the differential diagnosis.

There are a number of other conditions including ecthyma gangrenosum, ulcerative glandular tularemia, plague and even staphylococcal or streptococcal cellulites.

Now, the differential diagnosis of inhalational anthrax is long, includes a variety of agents that cause pneumonia, mycoplasma, legionella, psittacosis, tularemia, Q fever, viral pneumonia, histoplasmosis with mediastinitis is sometimes mentioned in the differential diagnosis as is coccidioidomycosis.

Patients who present with acute sepsis or acute meningitis, we should be thinking about that differential as was done in Florida, as was done in the Florida case.

And there are a number of other causes of pneumonia, which probably should be included in this list.

Now the diagnosis of cutaneous anthrax is made by the characteristic eschar. In addition, culture and gram stain of the sicular (sp) fluids are exudate. 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 with pleural effusions, blood or CSF cultures are positive and gram stain can be an important early clue.

Again, PCR, immunofluorescence and immunohistochemistry are important in establishing the diagnosis.

Now I've listed the current MMWR guidelines regarding post exposure prophylaxis to prevent inhalational anthrax. In adults, these are Ciprofloxacin or Doxycycline, 500 milligrams POBID of Ciprofloxacin, 100 milligrams POBID of Doxycycline. The current recommended duration is 60 days.

In children, again, the current recommendations are Ciprofloxacin, 10 to 15 milligrams per kilogram POQ 12 hours, or Doxycycline in the doses that are mentioned.

I will comment that these, this dosing schedule is available on the CDC Website.

I want to emphasize that sephosphorin (sp) should not be used in the treatment of bacillus anthracis infection as bacillus anthracis is resistant to sephosphorins.

Additional recommendations concerning prophylaxis to prevent inhalational anthrax will be forthcoming as additional data is developed.

Now the recommendations for initial anthrax treatment regarding acute inhalational or cutaneous exposure are listed on this slide.

Again, they include Ciprofloxacin or Doxycycline. Ciprofloxacin 500 milligrams, PO BID in adults or Doxycycline, 100 milligrams PO BID 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 the anthraces. The spore must be exposed to the anthraces spores.

To cause disease, 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:** David, thank you very much for that very comprehensive and very useful discussion. What we'd 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. BRADLEY A. PERKINS:** Yeah, thanks very much. It's a pleasure to have an opportunity to talk with all of you about the boundary between medicine and public health, and give you an inside glimpse at some of the strategies we're using to investigate these outbreaks and to help us to find the cases and the approaches we're going to recommend to identify people that are at risk and get them on appropriate therapy.

On October 4th, 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 in route to two locations that the case patients or the index patients had visited within the incubation period for inhalational anthrax--Florida and North Carolina.

This slide outlines the investigative strategy and early in the investigation the two 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.

That--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's 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, and 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're considering a confirmed case of anthrax to be a person that has clinically compatible illness with isolation of bacillus anthracis from affected sites or tissues, or two supporting non culture laboratory tests.

Now those tests may including staining with immunohisto chemical staining techniques, PCR studies identifying DNA of bacillus anthracis in clinical tissues or from clinical sites or cytology that suggests that there's been cyro conversion or strong cyro positivity to the anthrax organism.

For a suspected case, we're considering that there needs to be a clinically compatible illness and, in this situation, we don't have isolation of bacillus anthracis, but we had 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 that, 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 as 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 test that can serve as early confirmatory evidence of anthrax includes gram stains of affected tissues or sites, culture and we're 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's 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's necessary for rapid identification of persons that may be at risk for development of inhalational or other forms of anthrax.

Right now, we're 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 the confirmed vehicle--a letter that was positive for bacillus anthracis.

And lastly and most recently, in Washington D.C., we're presented with a situation where there's no obvious disease but a very recent exposure with a confirmed vehicle or letter.

This set of experiences is serving as the 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 bio-terrorism 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:** 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'd 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, the responsible government 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.cdc.gov/phppo](http://www.cdc.gov/phppo).

And by entering your location, you will be then 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'll provide information to you on how to link to that network system.

CDC also publishes a morbidity and mortality weekly report. I'd like to show you the copy that is now accessible over our Website. As you know, this journal publishes--The Journal of the American Medical Association reprints the NWR to facilitate distribution to you, and this week's issue features two important articles.

One, a summary of the investigation that Dr. Perkins just described and secondly, an article on recognition of illnesses that really relates to the issue of heightened surveillance.

Both of these articles are available now at our main Website [www.cdc.gov](http://www.cdc.gov).

CDC's also building partnerships with academic institutions, through 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'll 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 Website has it available to you.

Finally, we want to direct your attention to the part of the CDC Website 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 is, as he gave you earlier, [www.bt.cdc.gov](http://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'll not be able to respond to every question today, but we'll do our absolute best to use your questions as a guide in updating our Website and other information resources.

We're considering additional video conferences 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 that's come in is in doing that Florida investigation, when did you and your team first suspect that the two 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's 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 suspicions. This was the first case of report inhalational anthrax in the United States in more than 25 years old. 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 the state health department had revealed no obvious source for environmental or natural exposure for inhalational disease.

When we found bacillus anthracis spores in the index patient's workplace 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 clinched our suspicion, however, was the directed environmental sampling we did in the workplace, which revealed multiple bouts of contamination, the index patient's keyboard and the mail room and at that point the investigation became both a combined public health and a criminal investigation.

**DR. BAKER:** 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 post exposure antibiotic prophylaxis for prevention of inhalation anthrax in Florida. How'd you approach that?

**DR. PERKINS:** Well, for the last several years, we've worked at CDC and with many of our partners to develop recommendations for post exposure antibiotic prophylaxis. David Stephens has summarized those guidelines and they're 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. And those investigations are designed so we can identify everyone that's at risk.

As an adjunct to these investigations, we're 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've used have included nasal swabs for identification of bacillus anthracis in the nose. We've also used very targeted environmental sampling in environments we think may be contaminated with anthrax spores. And in some circumstances, we've actually obtained cytology to look for persons that may have been exposed to anthrax.

But I think it's important to note that all of these laboratory strategies, laboratory based strategies, are really an adjunct to the epidemiologic investigation. And there's been some confusion about the use of these tests in the situation and 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:** So it's not a simple decision. You have to integrate a lot of information in together to decide about when to start somebody on prophylaxis.

**DR. PERKINS:** Exactly. And one of the things that we're 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:** There's a question I think about antibiotic availability. People are certainly aware of the fact that the folks that purchase 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

were these antibiotics--they were given to individuals. Where did they come from, how were 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 the evening of Sunday evening, October the 5th 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 works beautifully and, you know, I'm sorry we had to use it, but it works very well.

**DR. BAKER:** So what you're saying is it took about ten hours, a little more than ten 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--even deliver earlier than that.

**DR. BAKER:** And as you know, that stockpile has also been deployed to other sites around the country in very short periods of time, just as was the case there.

**DR. PERKINS:** Exactly.

**DR. BAKER:** Another question that's come in has to do with this drug call 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 four-chronalone (sp) 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 includes gastrointestinal complications such as diarrhea and vomiting. In about one percent of patients, there may be some increased C&S irritability. But in general, Ciprofloxacin is a safe and effective antibiotic and has been used for some time.

**DR. BAKER:** What about other drugs? In your earlier presentation, you mentioned Doxycycline as a drug that's also been thought about, and other drugs that are there that have been mentioned in this context.

Could you say a little bit more about the risks 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. They also include issues of potential cartilage interference with ligament and cartilage formation in children.

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's also important that additional antimicrobe susceptibilities will help us determine other alternative regimens for both prophylaxis and treatment in children.

**DR. BAKER:** 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.

And 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.

And we'd like to see culture isolation from all of these, because we feel that that's the gold standard for diagnosis. But that's not possible in all circumstances, and we're fortunate to have a variety of other laboratory tools that will allow us to confirm cases of disease.

In the routine clinical setting, it's 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 argo (sp) plates that are used in essentially all clinical laboratories.

It's easy to get the sort of the bacillus level identification and, at that level, any bacillus species that is non-multile, non-hemolytic, that's growing under aerobic conditions should be quite suspicious in the setting of the clinically consistent illness and actually even that level of diagnostic confirmation should trigger reports to the public health system.

What's difficult is when you get beyond that. It's actually quite challenging to distinguish many of the other bacillus species from bacillus anthracis. And at that point, we have established, CDC has established, a network of laboratories, the Laboratory Response Network for Bio-Terrorism, 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 Bio-Terrorism.

These laboratories are all connected to CDC. They're using standard protocols and reagents that have been provided by CDC and other partners in bio-terrorism and they have the ability to confirm, in almost all instances, a identification of bacillus anthracis.

Now when we don't have culture, when we don't have an isolate, there's some other tests. These tests are less available in clinical laboratories and actually in some of the laboratory response network as well and they can be used to confirm cases, but they're 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 cyrology test, which is a research test that currently is only available at CDC.

**DR. BAKER:** What you described sounded to me like a sort of a three level system. In local hospitals, in local communities the capacity's there to basically identify the organism and that would lead the clinician then 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:** 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:** And that second level it's more the lab network--that's the more definitive identification, and the third level are those very specialized tests that you mentioned at the end.

**DR. PERKINS:** Yeah.

**DR. BAKER:** So it's sort of a three tier system.

**DR. PERKINS:** Yeah, yeah. That's exactly right, Ed.

**DR. BAKER:** Let's go on to some other issues here. There is a question that's come in regarding anthrax vaccine, whether or not it is available, whether or not it's the thing that should be done here in this setting.

Could one of you help us with the issue of anthrax vaccines?

**DR. STEPHENS:** Sure. There is an anthrax vaccine. It was developed through the efforts of the Centers for Disease Control some years ago in prevention of disease in settings where wool sorters disease in the 50's and 60's when that--where inhalational anthrax was a problem.

The vaccine is currently not recommended, except for those individuals who have, who work with bacillus anthracis. And Brad, you may want to comment on that issue.

**DR. PERKINS:** Yeah, I mean, the people that have generally been vaccinated with anthrax vaccine in this country are those people that have an occupational risk for exposure. At this time, it's--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:** And so basically what you're saying is the general population does not need to even think about anthrax vaccine. That's not an issue.

It's 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. STEPHENS:** Exactly.

**DR. BAKER:** Now, there are other people out there that, in their work, are concerned about being exposed to anthrax. For example, first responders, health care 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 are, 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 arm for use of licensed vaccines, entertains this issue in quite a substantive way over the last couple of years and there was a statement made by that committee that suggests that there's 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're seeing the occurrence of cases and the occurrence of risk and I think that, based on that change of risk, that we're going to have to reevaluate the need of pro vaccination in selected populations.

**DR. BAKER:** So we're rethinking that question in light of recent events basically.

**DR. PERKINS:** We are, we are.

**DR. BAKER:** A different question on nasal swabs. We've heard about nasal swabs. You did a lot of nasal swabs in Florida. That's happening now in various places around the country.

Maybe David, you can help us with this. What can you say about when it's indicated and when a nasal swab's really a need? What's the significance of that?

**DR. STEPHENS:** Well, 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 with that, Brad would agree with that, 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:** Would you say it's fair to say that a nasal, a positive nasal swab is really more a measure of exposure? It means that person's 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's exactly correct. Again, the decisions about antibiotic prophylaxis are driven by the epidemiologic investigation. And the nasal swabs, the environmental sampling and the potential cytology that's done are all adjunct 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, this one should not.

**DR. BAKER:** 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're learning some interesting things, learning some things about human nature. We've literally, in the context of the multiple investigations that CDC is currently involved with, we've 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's 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 office environments for example, and show it to people. We're finding that that's quite a frequent response to finding something unusual or something that people don't understand.

Secondly, we're 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. And 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's left there, that the person and anybody else in that room leaves the room and calls 911 for assistance.

**DR. BAKER:** Any further thoughts on that, David?

**DR. STEPHENS:** I certainly think that suspicion and notifying your state health department and following the instructions that Brad just gave you is sound advice.

**DR. BAKER:** Great. Well, I want to thank both of you for being with us today and also for all that you're doing on this extraordinary situation here at CDC.

Thank you for being with us today.

**DR. PERKINS:** It's a pleasure. Thank you.

**DR. STEPHENS:** Thank you.

**DR. BAKER:** That brings our program really to a close and I want to say that, at the completion of this broadcast, this program will be available online at the Website address that's on your screen, [www.cdc.gov/phtn](http://www.cdc.gov/phtn).

For further information on the health alert network that was mentioned before, there's 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 pm Eastern Daylight Time. At that point, please check satellite coordinates. They will be different for those today and, 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, and 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.

END

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