Webcast Transcript

CDC Responds: Coping with Bioterrorism—The Role of the Laboratorian

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Dr. Jeffrey P. Koplan:

Good afternoon, and welcome to our videoconference on "Coping with Bioterrorism—How Our Laboratories Are Responding." As recent events have shown so dramatically, we must be constantly vigilant to protect our nation's health and security. The war of terrorism is being fought on many fronts, and we must have a strong, robust public health system. This system must be on guard at all times to prevent and respond to multiple and simultaneous public health emergencies. Our system must include a strong core public health capacity in each community, combined with highly specialized expertise and facilities. Like our system of national military preparedness, our public health armaments, a skilled professional work force, robust information and communication systems, strong public health departments and laboratories, and effective private medical and community partnerships must be in a constant state of readiness. Because health threats know no boundaries, we can afford no weaknesses in our public health line of defense. Either we are all protected or we are all at risk. We must ensure that every health agency is fully prepared and that every community is served by an effective public health system.

That said, the recent bioterrorism events in our community have challenged both our medical care and public health systems, including our laboratories. There are areas of the country where the laboratory systems have been completely overwhelmed. Fortunately, state and local laboratorians, as well as CDC staff, have helped provide surge capacity. These challenges have made it clear that public health and clinical laboratories need to have well-established relationships and processes to ensure rapid detection and to provide timely and accurate information. While CDC can help provide leadership and technical assistance, the implementation must take place at the state and local level.

In New York City, current crisis response efforts have been bolstered by assistance from both the Department of Defense and CDC. In addition, the public health laboratory and the clinical microbiology community are meeting frequently to assure that capacity issues are being addressed. These meetings provide a venue to discuss laboratory needs as well as clarifying the roles that the broader laboratory community can play in addressing these needs. The experience in New York has made it clear that linkage among all labs and the rest of the public health system is just as critical as the technical capabilities of the labs themselves. Later in this videoconference, you will hear of similar efforts taking place in Minnesota, where the state public health laboratory is establishing links with 140 clinical microbiology laboratories around the state to provide health alerts and advisories, assess the capabilities of the clinical microbiology laboratories, identify gaps, provide training, and monitor the system.

While we will be focusing on addressing bioterrorism, many public health problems require high quality laboratory testing. Initiatives such as emerging infectious diseases, the epi and laboratory

strengthening program, the Food Safety Initiative, and the current bioterrorism program all rely heavily on a system that requires integration of the clinical and public health labs.

The broad base of clinical laboratories in this country is an essential component of our nation's public health and healthcare system. This component constitutes a public health laboratory system of its own. This conference is intended to help address questions from the clinical and public health laboratory communities. We intend to hold these conferences periodically to assure rapid transfer of critical information and to assure an opportunity for clinical laboratorians to ask questions and to provide comments to CDC. Thank you for participating in this important event.

Ms. Lisa Rayam:
As you've just heard from Dr. Koplan, the link between the clinical laboratory community and public health laboratories is an essential link in addressing bioterrorism. I'm Lisa Rayam, and welcome to "CDC Responds: Coping with Bioterrorism—The Role of the Laboratorian," which is the first in a series of programs that will be coming to you live from the CDC in Atlanta. The CDC is dedicated to keeping you, our audience, aware of the latest laboratory guidelines and procedures for addressing threats or actual events related to bioterrorism.

Now, before we continue, here are some important contact numbers you'll need if you have trouble receiving this program during our broadcast. For technical assistance in the United States, please call 800-728-8232. Our international technical assistance number is 404-639-1289.

And now, let me introduce you to Dr. Fred Tenover, who, along with our first panel of experts from CDC's National Center for Infectious Diseases, will provide an overview of laboratory issues for responding to bioterrorism incidents, and a preparedness guidance for all laboratories. Dr. Tenover, welcome, and please introduce your panelists.

Dr. Fred Tenover:
Thank you, Lisa. Today we are very pleased to have with us Dr. Tanja Popovic, the chief of the epidemiologic investigations laboratory at CDC; Mr. Richard Kellogg, the interagency liaison and CDC Laboratory Response Network coordinator; and Dr. J. Michael Miller, the chief of the epidemiology and laboratory branch. Our objectives for the program today are: to describe the laboratory tests used to diagnose the current cases of anthrax in the United States; second of all, to describe the structure of the Laboratory Response Network and the rationale for the Level A, B, C, and D laboratories; and then finally, to define the testing performed at the Level A through D laboratories, and the methods that are appropriate for specimen referral.

Tanja, let's begin with you. Tell us about the recent laboratory activities at CDC involving anthrax.

Dr. Tanja Popovic:
Certainly, Fred. Over the past 5 weeks during the ongoing anthrax investigation, professional lives of many laboratorians at 1600 Clifton Road have been drastically changed, and what I would like to do today is share with you an insight into those lives, into their long hours, into their struggles, obstacles, and the successes. I would also like to share with you an overview of

the CDC's laboratory capabilities at this time, starting with very basic microbiology procedures to state-of-the-art molecular diagnostic methods.

For us, it all started on October 3, 2001, with reports of suspected *Bacillus anthracis* isolates in Florida. And the very next day, the first CDC team, consisting of epidemiologists, laboratorians, and support staff was deployed to Florida. Two days later, as shown on this slide, 11 boxes with a couple hundred clinical and environmental samples came our way. This indeed was our "Saturday Night Live" for all of us who were there that evening. You can see our colleagues unloading these boxes and then taking them into our laboratories for analysis. One of many challenges that faced us at that time was to ensure very accurate tracking of all of these samples and the results that were done on them.

Here are some of our staff working on rolls of the CDC ID numbers, and that very first night we also had to set up our initial database.

These pictures were e-mailed to us from the Miami Public Health Laboratory, and they show the results of the gamma phage testing and India ink staining testing for one of the first suspect isolates. Shown here are the results done on the very same isolate at the CDC the next day, and you can see the results of the DFA (direct fluorescent assay) where we have confirmed the presence of both cell wall polysaccharide and capsule antigens.

This slide shows our initial organizational setup. All specimens were received at our Rapid Response and Advanced Technology Laboratory. There they were screened using rapid biodetection assays, such as PCR and time-resolved fluorescence. Then, specimens are forwarded to the anthrax laboratory for isolation, confirmatory testing, and molecular characterization. Biopsy materials and tissues, on the other hand, go to the infectious disease pathology activity, where recently developed immunohistochemistry assays specific to *Bacillus anthracis* were used.

I thought that it might be of interest to you to see what an average day in an anthrax lab looks like. So here we go. Specimens are first processed, and that means they're aliquotted—part of the specimen is used for molecular characterization and DNA is extracted first, while the other part is used for the standard microbiological procedures. Next is the work with the cultures themselves once the organism is growing, and that means performing presumptive and confirmatory testing. All records of the results and testing need to be sent out of the laboratory either by scanning the paperwork or by faxing it out so that nothing leaves our biosafety containment. Once that information is received outside of the Biosafety Level 3 laboratory, that information is entered into our databases, and then we can have reports and spreadsheets available to be shared.

Here is the work-up of a typical clinical material that came our way, and many of you who are working in Level A laboratories will be familiar with these methods. Initial work on clinical specimens includes Gram staining and India ink staining of blood for demonstration of the capsule. Once the organism is growing, it is very important to observe the typical colony morphology and especially the lack of hemolysis. Finally, *B. anthracis* is not motile, and that

characteristic is extremely helpful for differential diagnosis.

Now, here are the tests for confirmatory identification of an isolate as *Bacillus anthracis*. Lysis by gamma phage in conjunction with demonstration of capsule is the first confirmatory approach. Capsule can be demonstrated in several ways: by growth on bicarbonate-supplemented medium in enhanced CO_2 environment or by incubation in horse blood. Each then can be followed by M'Fadyean stain or India ink stain, as demonstrated on the slide. The second confirmatory approach is to detect both cell wall and capsule antigens by the DFA.

Work on the environmental specimens is somewhat different. Specimens can be directly examined for the presence of spores, either by the wet mount or malachite green stain. They can also be directly examined by the DFA for both of the earlier mentioned antigens. And finally, and understandably, microbiological media will be also immediately inoculated.

In addition to confirmatory testing of an isolate, a whole number and range of molecular approaches have been taken during this investigation. I have mentioned briefly that rapid detection assays such as PCR and time-resolved fluorescence are used in our Rapid Response and Advanced Technology Laboratory, and the PCR approach is also used directly on clinical specimens and on the cultures in the anthrax lab itself. Molecular subtyping of *Bacillus anthracis* is carried out by a method called MLVA (it stands for Multilocus VNTR Typing). It's a method that focuses on a number of specific targets in the *Bacillus anthracis* chromosome and two of its plasmids. It allows for identification of a particular pattern that can have association with geographic, temporal, or other relevant epidemiological designations, and this method has been extremely useful in the ongoing investigation. Finally, we're also conducting sequencing of the gene, coding for the 16S ribosomal RNA and a couple of other genes specific for *Bacillus anthracis*.

In addition to all of these activities, it became very soon quite clear that we needed to expand even further. So, the basic structure that we initially had was kept with Rapid Response Laboratory being the triage laboratory and doing the initial screening of samples. Most of the samples go into the anthrax lab for the isolation confirmatory testing and molecular typing, and then subsequently on for antimicrobial susceptibility testing. However, we have added activities in our microbial pathogenesis and immune response laboratory, where actually hundreds of sera were tested by serologic assays. And only last week, we have opened a surge capacity laboratory, our newest addition, so that large numbers of environmental specimens that are coming our way can be rapidly screened. To date, over 2,000 specimens have been analyzed at the CDC. From them, over 100 isolates have been confirmed as *Bacillus anthracis*. In many of these of specimens, presence of *Bacillus anthracis* was demonstrated by immunohistochemistry methods, and as I mentioned, many sera were shown to be reactive.

As you can imagine, a number of organizational and logistical issues had to be dealt with quite in a hurry, and some of them are the same ones that you are probably dealing with. If that is not the case, then this list might be very helpful for you to be prepared. As we moved on with our work, we had to develop protocols for collection of specimens that we never thought we would have to deal with, specimens like air filters, keyboards, clothing. And we had to develop protocols for

collection, shipping, and packaging of these specimens. Also, we rapidly had to expand from working a comfortable 5 days a week for 8 hours a day to working 7 days a week, 24 hours a day. You can envision that a number of additional staff had to be rapidly trained. We had to learn how to efficiently communicate with each other as well as with everybody else who wanted to communicate with us.

Finally, we had to learn how to keep the enormous amount of data that we were generating all the time in an understandable and manageable manner. As we continue to face new challenges, at the same time we also continue to be extremely encouraged by the strength of our laboratory network for which Level A laboratories serve as the wide and strong basis. The index *Bacillus anthracis* isolate was detected in one such laboratory and was then forwarded to the Level B laboratory in Florida where confirmatory testing was carried out. Shown in this picture is our colleague from that particular Level B laboratory, and the picture was taken exactly a year ago during the first of four bioterrorism preparedness laboratory trainings that we have conducted for laboratorians from throughout the country. As you can see, we have now made a full circle here, from isolation of a suspected isolate in a Level A laboratory, to talking to you today, again, about ever-increasing and important role that Level A laboratories play in the fight against bioterrorism. Thank you.

Dr. Tenover:
Tanja, thank you very much. Richard, can you describe for us now the Laboratory Response Network?

Mr. Richard Kellogg:
Yes, thank you, Fred, and thanks to all for this opportunity to speak today about the Laboratory Response Network. The LRN, as we call it, is a multilevel system designed to link frontline clinical microbiology laboratories and hospitals and other institutions to state and local public health laboratories in supporting advanced capacity public health, military, veterinary, agricultural, water, and food testing laboratories at the federal level. The key to the Laboratory Response Network is its partnership coalition, currently composed of clinical laboratories, state and local public health laboratories, the Association of Public Health Laboratories, the American Society for Microbiology, the Center for Clinical Laboratory Medicine in the Department of Defense, United States Army Medical Research Institute for Infectious Diseases, the Federal Bureau of Investigation, the Centers for Disease Control and the Food and Drug Administration, the Lawrence Livermore National Laboratory in the Department of Energy, the National Veterinary Service Laboratory, and the Environmental Protection Agency.

The LRN concept of operations is based on a system of safety and proficiency such that Level A laboratories at the BSL-2 provide the rule-out or referral of suspect specimens, with Level B and C labs at BSL-2 and 3 performing the rule in testing by rapid screening and confirmatory identification. Finally, Level D labs are reserved for the highest level of characterization and isolate archiving with BSL-4 capabilities.

An important point to remember is that the specific biological agent drives the challenges for handling, detection, and identification, and therefore, LRN laboratory ratings are actually agent-

specific. Whereas *Bacillus anthracis* and *Yersinia pestis* are confirmed at Level B, *Francisella tularensis* and the *Brucella* species are confirmed at Level C, and variola major, the agent of smallpox, is restricted to Level D. Future challenges for the Network involve other agents on the critical biological agent list, including the filoviruses Ebola and Marburg; the arenaviruses Lassa fever and Junin; the alphaviruses, causing Venezuelan, eastern, and western equine encephalitis; *Coxiella burnetii*; ricin toxin; *Burkholderia mallei*; and staphylococcal enterotoxin B. The Network structure, which gives us the needed flexibility, starts with Level A labs, which will be on the front line in a covert release, and as patients begin to present clinically, Level B and C labs will directly receive clinical specimens and environmental samples in an announced release, with Level D labs being able to support the Network as events require.

This map represents the approximately 100 Laboratory Response Network B and C level labs in 50 states which are in place to support the Network. The supporting B and C level labs are tied together by a secure Web site which facilitates access to specialized testing protocols, specialized test reagents, select agent test controls, a facility referral directory, and a proficiency testing program. Frontline Level A labs have access to rule-out and presumptive identification procedures, which use standard methods and which are available on the CDC Web site as well as the Web site at the American Society for Microbiology.

What are some of the important requirements for Level A labs? One is to maintain awareness. Much of that information can be found on the CDC Web site, which is listed below. Also, clinical laboratories with BSL-2 facilities should be using Class 2 biological safety cabinets, and be ready to safely perform rule-out testing on clinical specimens with standard methods. The methods are publicly available on the ASM Web site, and important safety guidelines on the CDC Web site are updated by the Office of Health and Safety. And then also, they should be ready to transport specimens and refer testing as needed to the closest state public health laboratory or other approved facility.

In wrapping up, I'd like to mention some of the 2001 objectives which we've been working on. First is transferring rapid technology (polymerase chain reaction and time-resolved fluorescence) to local LRN Level B labs for biodetection. We are also standardizing the testing algorithm at the suspect, presumptive, and confirmatory levels of agent identification for result reporting, as well as rolling out the proficiency testing to certify laboratory readiness for the specialized testing.

Lastly, I'd like to mention additional future objectives which are in progress. Those are supporting increased state-based training of Level A clinical laboratories; standardizing the notification schemes to communicate with the Laboratory Response Network and law enforcement, as well as enhancing the secure Web site to support secure communications, Web-based laboratory reporting, sentinel surveillance, and Geographic Information Systems, and most important, building the LRN partnership as a forum for input and planning.

Dr. Tenover:
Richard, thank you very much. Michael, now that we've seen the whole structure of the LRN, can you detail for us exactly what the responsibilities of the Level A laboratories are?

Dr. J. Michael Miller:
I think so, Fred. I believe we all know that the clinical microbiologists are really the cornerstone of this laboratory system.

This first graphic actually shows the two simple things that the Level A laboratory must be able to do. First of all, our job is to rule out *Bacillus anthracis* by simple observation. Ruling in implies an identification process that the Level A lab is not necessarily going to do. So we need to know and actually practice the safety precautions that are recommended for BSL-2 labs. Certainly know microbiology
observation criteria; in other words, be proficient at plate reading. And then know the limitations and the capacity of your own laboratory.

Secondly, it's very important to know when and how to refer any of these suspicious specimens to a higher-level laboratory. Knowing when to stop working on an isolate is many times more important than knowing when to start. Know where that next level is, whether it's the state public health laboratory and in what part of the state, and especially knowing the appropriate packing and shipping protocols is very important. It's not dangerous to work with clinical specimens if we follow those BSL procedures, and anthrax is no different. Anthrax as a disease is not contagious person-to-person. It's a BSL-2 agent, and the clinical specimens would be considered BSL-2 specimens. Now, if you're going to work with this agent in pure culture, if you're going to work with the spores in large numbers, then it becomes a BSL-3, but we're talking about clinical specimens at the Level A procedures. There's a low risk there, and if we follow the rules of BSL-2, we're going to be all right. Remember that spores of anthrax are usually not produced in the body or in tissue. And so, therefore, we will likely not be infected with spores by working with this tissue, particularly if we use the biological safety cabinet at the setup area as we are supposed to do. It lowers and eliminates most all of the laboratory risk that might be associated. Now, using 10% bleach as a disinfectant is what we recommend, and that bleach is going to kill most of the vegetative cells—in fact, it will kill all the vegetative cells and most of the spores.

The specimens we're most likely to receive from inhalation anthrax are likely to be blood, which would be the specimen of choice (that's the specimen that's most likely to be positive), and then sputum. Although sputum is not ideal specimen for anthrax, remember, anthrax is not a true pneumonia, so we're really looking for blood as our specimen of choice.

The laboratory handling really just needs to follow some very simple procedures. Keep in mind that working in the community hospital laboratory, we do not need anthrax vaccination; in fact, we don't need antimicrobial prophylaxis, even if we isolate an isolate of *Bacillus anthracis*. If we follow the BSL rules by wearing laboratory coats and gloves, particularly at the setup bench, and if you find a suspicious agent in the laboratory, that plate and all of its associated materials should go directly into the biological safety cabinet and further work should be done right there inside the cabinet. That would include preparing slides for Gram stain or motility, and certainly wearing gloves inside the hood if you're preparing the slide for motility. Washing hands is the classic procedure for safety, whether it's in the laboratory or outside the laboratory. So when we leave that laboratory area, make sure we wash our hands.

The specimens we're most likely to receive will be associated with the type of disease that's being presented. Anthrax may appear as inhalational disease, in which case blood would be the specimen of choice. Sputum may be requested, but still, blood would be our choice. Cutaneous anthrax is most likely to be isolated from vesicles and eschars, taken with swab specimens underneath the eschar. Gastrointestinal anthrax—blood again would be the specimen of choice along with stool to make sure that we have this organism.

For specimens that we have received a lot of questions about, let me mention one thing about nasal swabs as a screening test. This really should not be used for routine testing. It is not a valuable test, particularly for making decisions regarding patient care. The nasal swabs were designed to be used with support for epidemiologic teams who are in the field, or to evaluate known, documented exposures. So they are not to be used routinely. We don't even know how sensitive or specific the nasal swab is for detecting the spores of anthrax, so that's why we really do not want to use it. But you may be asked in some cases, and many of you have already, to work up a nasal swab (or a nares swab) for the spores of anthrax. If you do, just remember to use a noncotton fiber, use swabs either Dacron, rayon, or calcium alginate. Resist Gram stain requests on these specimens, because it's not going to be helpful in looking for spores of the agent. With a nares swab, if you are asked to work these up, we found that placing these swabs into phosphate-buffered saline, about 1½ ml, heat shocking them at 65 degrees for 30 minutes, and then plating on blood agar is an excellent way to determine if spores for this agent are present.

Now, there's another question that we've gotten quite often also, and I know you've faced it, too. It has to do with environment samples. What do we do with people who ask us to sample the environment? Let's talk about superficial surface swabs and separate that from other types of environmental samples. A simple superficial surface swab, just a tabletop or the top of a telephone, looking for anthrax swab may be acceptable in the Level A laboratory. There's no reason (for technical reasons) why you would not be able to do this. And I would recommend that if you are asked by your administrators to sample, for instance, your own mailroom or certain facilities within your hospital, that you could accommodate that, and it would be handled much the same way as you would a swab from the nose. A moistened swab over a specified surface area, take that swab in a small amount of saline and heat shock it and plate it. Very similar to processing nares cultures. But there's no indication that a community hospital should be in the business of sampling powders or bulk samples (such as office supplies, computer keyboards, water or clothing). Leave that to the authorities. If you have a question, call your state health laboratory and get information from them on what they recommend.

But what are you going to do in your laboratory? It's very simple. Tanja has alluded to this earlier. We need to do a Gram stain to know that this is a gram-positive rod. Understand the growth characteristics on blood agar where we're looking for a nonhemolytic bacillus colony. These organisms will sporulate in air. They are nonmotile, and in some cases you may want to look for the capsule by India ink or special stain. It's very simple. That's it; we do no more. If we get a suspicious isolate, we forward it to the next level laboratory for confirmation.

Now, let's take a look at the Gram stain morphology of an organism. The *Bacillus anthracis* cell is going to be a gram-positive rod that's 1-1½ microns wide and 3-5 microns long, and you may actually see them in chains. And, yes, you can view the Gram stain outside of the biological safety cabinet. These spores are oval, they are central to subterminal, and they do not significantly swell the cell. Remember, the spores are not going to be seen in a body specimen. Right out of fresh blood or out of tissue you're likely not to see a spore-forming bacillus. It's going to have to be incubated in air.

Here you see the picture of a typical Gram stain of a *Bacillus anthracis*. The colony morphology is very much like some of the other bacilli you may see. After 18-24 hours at 35 degrees, you're going to see in well-isolated colonies those that are about 2-5 mm in diameter. Keep in mind, this is really a rapidly growing organism. You don't have to wait for 24 hours to actually see the colony morphology. They are flat colonies, they are slightly convex, irregularly round, and the edges may be slightly undulate and often have little, curly, tailing edges, as you can see on this slide. Colonies have a ground glass appearance and kind of a sticky consistency. Now, this organism grows very well on blood agar and chocolate agar, even Martin-Lewis agar, but it does not grow on some of the inhibitory media, such as colistin-nalidixic acid agar (CNA); it does not grow in XLD, *Salmonella-Shigella* agar or MacConkey, and it does not grow on PEA.

This is an illustration of how the colony we describe as being sticky can be lifted with your inoculating loop. The edge of a colony can be lifted, and the colony many times will remain erect as you remove the inoculating needle or loop from under the edge of the colony.

So to summarize, here's an algorithm that illustrates how the Level A laboratory should respond to a request for culture for *Bacillus anthracis*. We're looking for large, aerobic, gram-positive rods, and there's only two simple tests we need to be concerned about after that. Is it hemolytic? If the answer is yes (and in this graphic, yes goes to the right and no goes down), if this organism is hemolytic, it's not going to be *Bacillus anthracis*; just report it as a *Bacillus* species. Motility can be done either using motility medium or you can use a slide motility. If the organism is motile, it will not be *Bacillus anthracis*. If it's not motile and it's nonhemolytic, then you'll certainly want to forward this isolate as suspicious to your state public health laboratory.

The safety issue is one that is absolutely critical, and you want yourself and everyone in your laboratory to understand the safety rules of working at the BSL-2 level. There are a number of Web sites that are listed on this slide that can be very helpful to you, both from CDC and items on packing and shipping. If you do have questions, the first source you might try is going to be your state public health department.

Dr. Tenover:
Michael, thank you very much.

Ms. Rayam:
I would like to thank you all for your very timely and very important information contributing to this very important discussion on the effectiveness of the laboratory, safety precautions, and testing. Dr. Tenover, I'd like to take this a step further with yet another question that might spark

some more discussion. How is the CDC determining what antibiotics are effective for treating these anthrax infections?

Dr. Tenover:
Lisa, it's very important to note that there is no standard method yet defined for *Bacillus anthracis* testing. So here at CDC we're using the reference broth microdilution method as defined by the National Committee for Clinical Laboratory Standards. So far, of the 15 clinical isolates of anthrax that we tested from the U.S., all have been susceptible to penicillin, doxycycline, and ciprofloxacin. At this time, however, we are not recommending that other laboratories, including state health departments, do this testing, and there's really 3 reasons: the first one is one of safety. It's very important to recognize that susceptibility testing potentially could produce aerosols. So we do this testing in a Biosafety Level 3 laboratory in a biological safety cabinet.

The second one is a scientific one. That is, we are still understanding the ways that this organism can become resistant to antimicrobial agents, and the optimal method for testing has not yet been determined. So we hope to work out these procedures, and at that point we will reconsider disseminating the methods to other laboratories.

The last one really is the practical issue, though, and that is we have evaluated alternate methods of susceptibility testing that potentially could be done within the safety cabinet. However, at this point none of them reflect the methods and the results that we get by the broth microdilution reference method. So right now, again, that is the method we are using here at CDC.

It raises several other questions, though, that we've received during the past week, and I'd like to share some of those with our panel. Again, Tanja, let me start with you. We've had a lot of discussion about typing, molecular subtyping of this organism. Can you comment on the use of pulsed-field gel electrophoresis or ribotyping or other molecular methods?

Dr. Popovic:
Certainly. I think we can all appreciate the importance of the issue of molecular typing at this time, because that is the approach that allows us quite frequently to trace the origin of organisms in question. Let me start by saying that *Bacillus anthracis* is extremely homogeneous. A number of methods, including those that you have mentioned, have been tested and tried. Unfortunately, it seems that all organisms—all *Bacillus anthracis* organisms—when tested by these methods look either identical or very much alike. So it does not appear to be a lot of differentiation potential. As I have briefly mentioned, therefore, currently the method of choice is multilocus VNTR typing approach, in which we focus on a number of chromosomal and plasmid targets, and we come out with a pattern that can then later be associated with temporal or geographic or other relevant epidemiological markers, and this method has been used again in a real-time manner throughout this investigation, and we have found it to be extremely useful.

Dr. Tenover:
Good, thank you. Richard, in your presentation you mentioned that some states have more than one Level B laboratory. So how do we know which specimen to send to which laboratory?

Mr. Kellogg:
Well, yes; in general, most states have more than one B level laboratory. For example, Texas (for *Bacillus anthracis*) has eight. There are B level laboratories, though, not only at the state level facilities, but also at large city and county public health laboratories, and federal and military facilities as well. By contacting your state public health laboratory director, your closest B level facility can be identified in advance. Always keep in mind that the designation, the rating is agent-specific.

Dr. Tenover:
Good, thank you. Michael, we received a lot of questions from Level A laboratories about how do we disinfect our benches, and do we need to do special autoclaving to get rid of these samples? Can you comment about using bleach versus maybe a quaternary ammonium compound for disinfecting lab surfaces?

Dr. Miller:
Sure. A lot of people are really concerned about how to take care of their disinfectant issues here. We recommend a 10% solution of household bleach, and that's simply made by one part bleach into 9 parts of water. This takes care of virtually all vegetative cells. While it's not by definition a sporicide, it actually reduces the number of spores 3 to 5 logs. Now, quaternary ammonium compounds, alcohol, other normal hospital disinfectants are not effective against these spores, so we are recommending the 10% bleach solution.

Now, what about autoclaving? In our laboratories, we for our own purposes use a one-hour autoclave time, but that's because we have large loads and large amounts of potential anthrax inside those loads. But the clinical laboratory need not vary from the routine 15-minute autoclave time that they're using now. That should adequately kill the spores of *Bacillus anthracis*.

Dr. Tenover:
Good, thank you. Tanja, in the news there's been a lot about hand-held devices for finding spores in the environment. Recently we heard about a new PCR test from the Mayo Clinic. I wonder if you could comment about these procedures?

Dr. Popovic:
Well, this is certainly not an unexpected question and I'll be happy to comment. I'd like to make a distinction between the hand-held devices that are primarily used to detect spores of *Bacillus anthracis* in the environment and those PCR-based tests that are used to detect genetic material of *Bacillus anthracis*, either directly, in clinical specimens, or on the growing culture. Regarding hand-held devices, CDC is not recommending use of these hand-held devices for testing environmental samples. Data that is currently available and provided by the manufacturers of these devices suggests that the number of spores necessary for the test to be positive is very large, and they go up to 10,000—in the range of 10,000. And while that might be of value in heavily contaminated areas or samples, we might actually miss areas where that level of contamination is not so high. So CDC has been asked to assist in validation and evaluation of these assays. As soon as the studies are underway and completed, the results will be shared.

The second is the comment about the PCR assay such as that as reported by the Mayo Clinic. I'd like to say, over the past 2 years, we have worked with a number of partners and have developed a PCR-based assay that has proven to be extremely sensitive and very specific that has been used for the past 5 weeks intensively, primarily in our Advanced Technology Laboratory that serves for that screening purpose. And, specifically, about the Mayo Clinic assay: just like any other new assay, it does need to be compared to the assays that are already available, and until such tests are done, it is very difficult to talk about specificity, sensitivity, and appropriateness of a general use of these assays.

Dr. Tenover:
Good, thank you. Michael, maybe we can talk a little bit about environmental sampling at the Level A laboratory level. What are sort of the boundaries if the laboratory director is approached by the hospital administrator and wants to have their mailroom cultured? How would you advise these people, the laboratory directors?

Dr. Miller:
Well, the good point is that you're approached by your own management, and I believe if that's the case, where you have been asked to sample an area within your own hospital where there's a low risk or no risk, then probably it's okay to provide this type of sampling. And all this would mean would be using, again, a non-cotton swab that has been moistened, rubbed over a specified area of a tabletop or a mailbox or whatever you're sampling within your institution, taken to the laboratory and heat shocked in 1½ ml of saline, and then plated. The heat shock takes place at 65°C for 30 minutes, then you plate 100 microliters. That's what we do. Now, I don't think at this point that hospitals at all should be taking on specimens from which there really may be a credible threat, or we just don't want to bring into the hospital laboratory (or into the facility where our patients are) specimens that may likely be contaminated with anthrax spores. So if we're going to do environmental sampling, it probably needs to be done within the institution, and management certainly needs to be involved in that decision.

Dr. Tenover:
Good, thank you. Our last question goes to you, Richard, and that is sort of a follow-up to what Michael just said. What problems would you see in performing Level B type of activities in a Level A laboratory?

Dr. Kellogg:
Well, I really do want to reiterate what Mike has said, and that for *Bacillus anthracis*, the LRN does not recommend that clinical labs, especially those located in patient care facilities, pursue LRN B level status and high-risk environmental sample testing. The LRN has particular concerns about potentially high-risk environmental samples, such as spore powders, especially those that could further contaminate and cause contamination problems in a facility. Other environmental samples not related to a credible threat assessment or established area of exposure may be done at Level A labs. But again, this should be very low-risk work, often taken to calm people's fears, and again, at the discretion of the laboratory management.

Dr. Tenover:
Good. Thank you all for your responses.

Ms. Rayam:
Again, thank all of you. Very timely responses during a very critical time in America. Thanks to you all.

Ms. Rayam:
Welcome back to "CDC Responds: Coping with Bioterrorism—The Role of the Laboratorian." In the first half of today's videoconference, we heard about the impact on the U.S. of recent bioterrorist events associated with anthrax. We also heard about the Laboratory Response Network that has been established to assure availability of appropriate testing across the country, and we talked about the role of Level A laboratories and how clinical laboratories in this country form the basis for the Laboratory Response Network. Now we'd like to talk about some real-life field experience, and we've invited Dr. Robert Martin, director of the Division of Laboratory Systems at CDC; Dr. Susan Sharp, director of the Clinical Microbiology Laboratory, Mt. Sinai Medical Center and Miami Heart Institute; and Dr. Norman Crouch, director of the Minnesota Public Health Laboratory, to talk about their experiences with these events. When it comes to events like these recent bioterrorism activities, we can understand how important it is for clinical laboratories to interact and talk to their counterparts in public health laboratories, to get information about how to deal with new public health issues that are dependent on laboratory information.

Dr. Martin, welcome. I'd like to begin by asking you to explain how the clinical laboratory and the public health laboratory normally interact.

Dr. Robert Martin:
Thank you, Lisa. That's a good question, and the answer is somewhat dependent on the policies and practices that have been established in each state. Let me give you an example. Our division provides consultation services to public health laboratories across the country, and I was recently working with the Department of Health laboratory in New York City. It was gratifying to see that the public health and clinical community in New York had established an advisory council made up of the directors of hospital microbiology laboratories around the city. In times of crisis, having venues like that for discussion become even more important. Around the country, there are some important efforts underway to help us address improvement of collaborations and communications between clinical and public health laboratories.

I'd like to call on Dr. Susan Sharp first to talk about the experiences of a large clinical laboratory during these recent events, and then ask Dr. Norman Crouch to talk about how the public health laboratory is addressing these issues in Minnesota. Dr. Sharp, can you tell us about your laboratory's experiences during these events?

Dr. Susan Sharp:
Certainly, and thank you, Dr. Martin. Over the next few minutes I'd like to try to give you an idea how the Level A laboratories have viewed and dealt with the current anthrax crisis. And I'd

like to start by reviewing how the Level A laboratory in south Florida handled the first inhalational anthrax case.

It was Tuesday, October 2, early in the morning. The onsite immediate response laboratory of this Medical Center reports that they had a spinal fluid that contained white blood cells and gram-positive rods. The specimen was then sent to the main laboratory. About 10:00 that morning, the offsite main microbiology laboratory speaks to the ER personnel to report that they had a Gram stain that was consistent with *Bacillus* species which was nonmotile by wet prep of the spinal fluid. About 11:00 that morning, an India ink preparation was made from the spinal fluid, and it was determined at that point the organism was negative for capsule formation. About 3:00 in the afternoon, the isolate was already growing on a blood agar plate and was shown to be nonhemolytic. The laboratory then mailed the organism by overnight courier to the Jacksonville laboratory in northern Florida.

On Wednesday, October 3, at 8:00 in the morning, the main microbiology laboratory noted that central spores had formed in the organisms that were growing on the culture plates. By 11:00 in the morning, the Florida Department of Health had received the organism.

By the next day, Thursday, October 4, in the morning, the Florida Department of Health reports to the CDC and the FBI that the definitive tests confirm that the isolate was a *Bacillus anthracis*. In the afternoon of October 4, the submitting laboratory in south Florida finds out the identification of the organism from a television news report.

So what worked in this scenario? The Level A laboratory response was excellent in this case. The organism was identified as a possible *Bacillus* species from the Gram stain the same day the spinal fluid was submitted. The organism was shown to be nonmotile and nonhemolytic, and at this point capsule-negative; again, the same day the spinal fluid was submitted. The organism was forwarded to a Level B laboratory the same day that the specimen was submitted. And by the next day, the organism was found to form central spores.

Now, what didn't work in this case? As you can see by this graphic, the submitting laboratory was located just north of Miami in Fort Lauderdale. They sent the organism by overnight courier to the Jacksonville laboratory in north Florida, which was approximately 300 miles away. Unbeknownst to this laboratory, there was yet another Level B laboratory that was located in Miami, almost 25 miles to their south, so not a very far distance away. They could have had the specimen to a Level B laboratory one day sooner. This would have allowed for the identification of the organism 24 hours sooner. So a recommendation might be to have more visibility of our Level B and our Level C laboratories. Also what didn't work in this case is that the public health officials did not report back to the submitting laboratory the identification of the organism in a timely manner. The public was informed of the confirmed anthrax case before the submitting laboratory was informed. This caused somewhat of a loss of credibility of the laboratory management staff with the technical people in the laboratory. And the laboratory felt they were very needlessly kept out of the loop by the public health officials. So another recommendation would be to have more effective and timely reporting back to the submitting laboratories.

A big concern at the Level A laboratories was with communications. Level A laboratories were being inundated with telephone calls requesting information. These calls would come from doctors, healthcare providers, our medical center administrators as well as our security departments, and a wealth of phone calls were also coming in to Level A laboratories from the public. No information was forthcoming rapidly from the public health sector to the Level A laboratories. Some information may have been provided to infection control practitioners in our institutions, but again, the laboratory felt they were left out of the loop.

It was very difficult for Level A laboratories to initiate contact with the public health sector. It was very difficult to actually speak to a key person within the framework of the Laboratory Response Network. Oftentimes no one answered the phone, and this was especially a problem after hours and on weekends during this crisis. If you did get through, oftentimes you got a voice mail, the voice mail oftentimes was full, and you could not leave a message. If you were able to get through and actually leave a message, very few of these phone messages were actually returned in a timely manner.

And then, of course, there was the issue of the nasal swabs, which we all had to deal with. We had no early guidance on whether Level A laboratories should provide anthrax cultures from nasal swabs. Again, as mentioned earlier, we know that the sensitivity and specificity of this assay were unknown. We didn't know whether people that were possible exposures or the "worried well" should or should not be cultured, but we did have doctors insisting that these cultures be performed, and yet we had no ammunition from the public health departments to try to deter this practice.

There was also sometimes contradictory information received from the public health sector. The Department of Health would state, for example, that nasal swabs should not be done, and then we would hear from the local public health epidemiology department that if a doctor orders a nasal swab, it should be performed at the Level A laboratory. So another recommendation would be to expedite the verbal communications coming from the Level A laboratories, and perhaps designating personnel from the Level B, C, and D laboratories for this purpose would be beneficial. In addition, more effective information flow to all Level A laboratories is also necessary.

Another concern of the Level A laboratories is with education. We need to ensure proper education of all Level A laboratory staff. We need to procure funds for the education of the Level A laboratories, which is crucial for the functioning of the Laboratory Response Network. We need to promote the recognition of bioterrorism agents in the Level A laboratories, perhaps by using avirulent strains or perhaps strains that would mimic bioterrorism organisms in some kind of a proficiency testing survey. So another recommendation is to move forward with bioterrorism training for all Level A laboratory personnel throughout the country.

Another Level A laboratory concern is with our participation with the Level B laboratories. There have been reports that testing of suspicious isolates may be taking too long at some Level B laboratories. Some Level B laboratories, as we heard earlier, can become overburdened by the amount of material that they're receiving, which is an overwhelming amount. Credibility could

become an issue with the delay in the testing of samples, and, lastly, but certainly not least, the public's health could be possibly compromised by prolonged turnaround times of these test results. In our Level A laboratories, there is a wealth of bioterrorism expertise that already exists. There are very qualified and technically skilled individuals working within the confines of the Level A laboratories, and the infrastructure also exists to support working with the agents of bioterrorism in some of these Level A facilities. The identification of individuals in the Level A laboratories that are capable of training additional Level A laboratory staff as well as assisting the public health system with the threats of bioterrorism would be beneficial to the entire laboratory response network. The laboratory response network is now several years old, and its structure is currently in a state of flux and constantly renewing itself. The laboratory response network may need to be re-examined and perhaps retooled in light of the present circumstances. So our final recommendation would be for more community laboratories to be designated as B or perhaps a new level of designation of AB. These would be community laboratories that would have the training and the expertise to assist the Level B laboratories when the need would arise in functioning in a bioterrorism crisis.

So, in summary, there are three recommendations: first and foremost is communication from the top down to the Level A laboratories, we must have communications. We also need to have effective ways for the Level A laboratory to communicate back to the public health sector. Secondly is education. We need to have education for all personnel working in the Level A laboratories, and I'm happy to report that the National Laboratory Training Network has plans to more aggressively pursue this training in the future. And last would be the participation of selected Level A laboratories with the public health system to assist with the burden of bioterrorism during a crisis situation. Thank you.

Dr. Martin:
Thank you very much, Susan, for sharing that information with us. That was really important information from practical field experiences. Norman, what I would like to do now is as you to talk about one of the more important issues that we've heard here and that is issues related to communication. Oftentimes we hear a lot about technology and the importance of implementing technology, but we've also heard here today that communication issues are critical for the public and federal laboratories to relate to the hospital laboratories. Can you describe some of your recent experiences and what steps have been taken in Minnesota to address those issues described by Dr. Sharp, including what you're doing about improving communications between public and private laboratories?

Dr. Norman Crouch:
Yes, thank you, Dr. Martin. I'd be glad to. Let me point out first, however, that each of the 50 state public health laboratories is a Level B facility, either for all the agents or at least for some of the agents. Some of these are actually level C laboratories and as such, it's very important that each of the state public health laboratories realize that they have a very essential role to play in the laboratory training network.

On my first slide, I want to talk about some of the kinds of materials that we get in the state laboratory to test, as I want to point out that the public health laboratory, its main role, or one of

its main roles, is to confirm the existence of a bioterrorism agent in materials that come into the laboratory. The referred isolates are isolates that we receive from clinical laboratories, the Level A laboratories, where they have isolated an organism that they cannot rule out as a contaminant. So it's sent to our laboratory to determine if it is in fact a bioterrorism agent. We also get environmental samples, and the environmental samples are generally brought the state laboratory by public safety. This can be the fire or police personnel or it can be other federal agencies. We get also powders to test for anthrax spores; certainly the last few weeks this has been a real concern. And I want to point out, again, it's been mentioned before, that these are potentially very dangerous materials, and they should not be handled in Level A laboratories. It's required, or it's certainly recommended, that these only be handled where there are BSL-3 conditions.

Finally, the clinical specimens that we receive in the Level B laboratory or the state laboratory are materials that are sent to us directly for diagnostic testing. And this happens when we have an outbreak, if we have a concern about bioterrorism, or actually there are patients who are becoming ill. This certainly has not happened to a large extent in this current situation, but if a major attack would occur. These are specimens that are not sent to the Level A laboratory, but they're sent directly to the state laboratory for confirmation and testing for diagnostic purposes.

On this next slide, I want to point out that the state laboratory really plays a pivotal role in the LRN. It, on the one hand, works closely with the Level A laboratories, and, on the other hand, it works directly with the CDC to implement federal recommendations for laboratory practices, and also to implement new methods that are being brought to us from the CDC and their research laboratories. As shown on this slide, the role of the state lab is to first of all confirm suspicious isolates found by the Level A labs in their communities. This is a very important role, of course, for the Level A laboratories. In doing so, the public health laboratory is responsible for accurate and timely reporting of the test results, and they provide this data to the public health officials, and this assures rapid intervention and prevention—for prevention and control. And as Dr. Sharp pointed out, it becomes very important that we not only report to our own—within our own health department but we also need to report back to the Level A laboratories what we have found in our confirmations investigations.

A second part of what the state laboratory does, in addition to testing, is to provide information and guidelines to the Level A laboratories. In Minnesota, we provide the Level A laboratories with community alerts to keep them up to date on what is happening in the community, and particularly what is necessary for them to know regarding laboratory testing. We provide them with technical information, and we provide them with assistance that they may need to have to decide what kind of required actions they might need to take. If a laboratory in the Level A category, the clinical laboratory, has any questions, they should call the state laboratory to get assistance.

Another area of the state laboratory is to effectively facilitate communication. As Dr. Sharp mentioned, communication is really a very key component here. If we're going to have a network where we interact between public health laboratories, state laboratories and the clinical laboratories out there on the front line, we have to have excellent communications. It has to be between the state laboratory and the clinical laboratories. It also has to be clearly a good

communication between the state laboratory and the CDC. The state laboratories have a key role in developing a strong intrastate network between the clinical and public health laboratories. This is what we really are trying to do in Minnesota, is to try to establish an integrated network to make this work well.

These are the key elements that I put on this slide that I think are important in developing this kind of interactive intrastate interaction and laboratory system. In our state, we are trying to address each of these. The first is a statewide database. We're trying to build this through a comprehensive survey being done with all of our Level A laboratories in the state.

Secondly, we're trying to develop a communications system that is multifaceted and also very robust, and we're trying to develop a courier system. This is a continual problem state laboratories, to develop a courier system that is reliable, that transports materials and samples and referral isolates and such from Level A laboratories to the public health laboratory.

And finally, we're working hard to develop a surge capacity plan. If we're faced with a situation where we have a major attack, it's going to be very important to have something in place to be able to deal with this. We can't do it retrospectively, but we really need to take proactive action. Now, I'd like to discuss each of these separately.

First of all, Minnesota is developing a comprehensive statewide database of all the Level A laboratories in the state, and that includes all of our clinical as well as public health laboratories other than the state laboratory. The first part of this is to develop lab contact information. We need to know who are the key contact persons in each lab, their phone, their e-mail, and their fax numbers and also, if it's very important (I think Dr. Sharp mentioned this) that the Level A laboratories also need to have this kind of information. They need to have phone numbers of people to contact at the state laboratories so when there are questions or concerns or an emergency, they know where to go. So in Minnesota what we've done is we've provided a laminated list of key phone numbers and key personnel to all of our Level A laboratories so that they know where to call.

A second part of this is personnel experience in the statewide database. We want to know what is the level of staff training in these laboratories in the state and what kind of technical expertise is available. As Dr. Sharp mentioned, there's a lot of technical expertise in these clinical laboratories. It's important for the state laboratory to know what these are and where they are. Laboratory capability and capacity is another important item. What is the technical capability of the various clinical laboratories? And what are the lab's capacities to increase this activity in case we would have a situation where there is a need for expanding our surge capacity, and, finally, our communication capability, and that's the kingpin that we've talked about here. We need to find out what our clinical labs—what is their capability to communicate with the state lab? Do they have access to the Internet? Do they have e-mail? Do they have fax capabilities? And it's not always the case, and we need to know that and add that into our database.

Secondly, we're developing in Minnesota an effective communications system between all of the clinical laboratories and the state laboratory. First of all, we are trying to develop very broad-

based e-mail and broadcast fax capability. We want to be able to reach all of the Level A laboratories, and in doing so not just getting the information out there and wondering if it actually got to these laboratories, but having a way of knowing whether this communication has really reached all of the laboratories that we're trying to reach.

A second part of this is the Health Alert Network. Now, the Health Alert Network is not part of the LRN, this is separate, but we are using this in Minnesota, because we do have a robust Health Alert Network, and we're trying to use this as also a way to communicate with our clinical laboratories. The Health Alert Network was originally set up to provide electronic communication infrastructure between the state health departments and all of the local public health agencies. But we have found that we can add on to this group, the public health and the clinical laboratories in the state, which will then provide us with an ability to provide them with clear, short laboratory alert messages and concise information and recommendations, and it really will facilitate our ability to communicate, Another part of this, and linked to the Health Alert Network, is the use of a secure Web site so that we can put on this Web site, password-protected essential information that we might need to get out to the laboratories.

And finally, active surveillance. I want to just give you an example of active surveillance that we've put in place using this kind of communication network in Minnesota. With the situation that is occurring, we are now in a situation where we have active surveillance for gram-positive rods in Minnesota. And we are sending out a message every morning to all of these clinical laboratories to ask them to report back immediately, to find out if they have isolated any gram-positive rods that might be contaminants or they might in fact be isolates of *Bacillus anthracis*. We are doing this in a way that we can get a quick request out there and a quick reply back. We hope it's meaningful, and we hope it also will become habit forming. I say habit forming not in jest, but I think that's what we're faced with. We need to develop communication systems that are routine and every day; there's an expectation of communication.
Next is the reliable courier system. In Minnesota, we're trying to establish a reliable courier system between the Level A laboratories and the state. And this is essential for the network, but there are problems with the current system, and this is probably the case in most states. One of the problems is the scheduled transport. When we try to rely on scheduled transport where a clinic may have a pick up early in the morning, and if we miss that we might have to wait another day before we can get the material we need, it may cause delay if the pick up is missed, so we need to have some kind of on call backup in place.

Another problem is remote out-of-state services. In the rural areas it's very problematic to getting access minimums and such to the state laboratory. This can cause significant delays and specimen compromise if there are extended delays.

Finally, multiple couriers per sample. In some of the situations, particularly remote areas, couriers pass off a sample from one to the other, and samples can get lost and also samples can be delayed in getting to the state laboratory. What is needed is a well-defined courier system that will ensure delivery at any time. Finally, we're putting into place a surge plan so that the state laboratory can quickly expand its capacity to handle an extremely large volume of testing.

The development of this plan hinges on what I've just talked about: a statewide database, having a statewide database, having an effective communication system, and also having a reliable courier system. We're interested in looking at facilities. The state lab might not have enough space to conduct all the necessary testing. We need to prearrange this. Confirmatory testing might be delayed. We need to have prearranged ability to utilize appropriate additional laboratories, either Level A or extending some of the Level A to Level B capabilities. Personnel recruitment, we need to have in place the ability to recruit additional staff. We might have space but might not have the staff to do all the testing.

Emergency training—If we're going to recruit additional staff from other places, we need to be able to train them quickly. We're preparing a CD-ROM for this purpose and also developing a rapid training format.

And, finally, reagent distribution. If there would be a surge, would need to be able to contact the CDC to acquire additional reagents that might be necessary for dealing with the surge. Finally, from the state laboratory perspective, at least the one I'm talking from, the LRN is becoming a very powerful network, but there still remain some challenges. One of these challenges is the communication capabilities. What we have found in Minnesota, that the clinical laboratories vary greatly in their communication ability. Some differ markedly. And so we have to try to link all of the laboratories in a way that we can really completely build this robust communications system.

Another problem with is with out-of-state laboratories. Many clinical laboratories submit specimens that go out of state to these large commercial laboratories, which do an excellent job, and these are actually Level A laboratories, but we have a problem with a loss of the rule-in isolates. If they find what they consider to be a contaminant, it's not sent to the state laboratory for further analysis. And so we need to correct that by developing a relationship with these large commercial laboratories. And finally, sustained collaboration. In order to have a laboratory network where we have an integrated system of the public health laboratories and the clinical laboratories, we have to work on a system that we can sustain. And I think one way to do that is to develop the laboratory, the national laboratory system where we have a system where we have an integration of the clinical laboratories in the state with the public health laboratories so that we can meet the needs of an attack that might be perpetrated upon our country. Thank you.

Dr. Martin:
Well, thank you very much, Norm. We have time for just a couple of questions each, and Susan, I'll start with you. You touched on a number of very important issues in your presentation. Maybe the first question would be—how does a laboratory become identified as a Level A laboratory?

Dr. Sharp:
Well, that's good question. First of all, the fact is you don't have to wait to be identified as a Level A laboratory. If you're a laboratory that performs diagnostic testing in a clinical setting for human disease, you are a Level A laboratory by default. There are no inspections or certifications that will be done by the CDC or the public health authorities.

Dr. Martin:
Thank you. Norm, a question for you. One of the concerns we all have is what happens if this event becomes even more widespread or if a subsequent event becomes more widespread—could the CDC provide enough confirmatory reagents to meet the demands of Level B laboratories?

Dr. Crouch:
That's an important question. And the answer to that is in the present situation the CDC has thought about this, and they have decided to increase at least twofold the availability of these reagents or the amount of these reagents that are available. And so in that situation, if there would be a large surge, what the CDC will do is provide the emergency response and target it to the areas of the country where the surge is the greatest, so that they can utilize the additional reagents effectively.

Dr. Martin:
And, Susan, if all of the clinical microbiology laboratories in this country are potentially Level A laboratories, how will training be provided to such a large audience?

Dr. Sharp:
Well, in some states, the public health laboratories have already sponsored a number of Level A training sessions. The National Laboratory Training Network has provided 95 different courses to approximately 5,000 participants since January of 1999. Now, granted, a lot of these participants were Level A laboratory personnel, but there's still a lot of work to be done in this area. To this effort, currently, every laboratory that subscribes to a higher proficiency testing sample in the United States will be receiving or has already received a two-tape video and a CD-ROM that's produced by the National Laboratory Training Network for the purpose of educating Level A laboratory staff. In addition to this, you can find additional information for training and protocols on bioterrorism on both the CDC and the ASM Web sites.

Dr. Martin:
Thank you. And the final question for Norm, as we mentioned earlier, safety is always something that's uppermost in our minds when working in the laboratory. If laboratories working with culture isolates at the bench, for example, in a Level B laboratory where you're actually trying to rule in or rule out anthrax, should one receive antibiotics or vaccine? I know Dr. Miller addressed this a little earlier, but I would like you to reemphasize that point.

Dr. Crouch:
Dr. Miller did address this. If you're working in a Level B laboratory where you may be working with powders, you're working with a wide variety of samples and materials, as I indicated in my first slide, then the recommendations may become that we will in fact need to vaccinate individuals that work in those situations. Because there is some risk. While this is a level 2 agent, when we're working with large amounts of material that we can't be sure about, it would be expedient to do that.

Dr. Martin:
Thank you. As we have heard from Dr. Koplan and from our panelists, the link between the

clinical laboratory community and the public health laboratories is an essential link in addressing bioterrorism. At CDC, we're currently working on the development of the concept of a national system of laboratories that brings existing public and private laboratories together in a closer working relationship. That link is also essential for many public health initiatives, including emerging infectious diseases, food safety, HIV AIDS, and many other programs that effect both individual health and the health of the community. The concept of developing better bi-directional communication with the clinical laboratories is the focus of the National Laboratory System. In addition to the project in Minnesota directed by Dr. Crouch, we have three other projects in Washington, Nebraska, and in Michigan. Working within these states, the public health and clinical laboratories are developing partnerships, assessing capabilities and capacities, determining laboratory work force training needs, and developing standards to ensure comparability of information. Included among the consultants for this initiative are many of the organizations that co-sponsored this videoconference. Again, working with our partners, we hope to extend this concept nationwide so that every state becomes involved, thereby establishing a true national laboratory system. With closer working relationships, initiatives such as the important one we are all involved in now, bioterrorism, will be addressed in a manner that assures availability of consistent laboratory capacity for public health across the nation. Thank you. Lisa?

Ms. Rayam:
Dr. Martin, thank you. And thank you, panelists, for your timely information during this timely crisis in America. Thank you all. And I'd like to thank you, our audience, for joining us for this, our first program in a series that will deal with important public health issues. Please join us again next Friday for our next CDC response program, bioterrorism and the infection control community. On behalf of everyone at CDC and the public health training network, I'm Lisa Rayam, wishing you a good day from Atlanta.