COCA Conference Call
Overview of Bioterrorism Agents
CDR William Bower, MD
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Coordinator: Welcome and thank you for standing by. At this time all participants will be in a listen-only mode. After the presentation we will conduct a question and answer session; to ask a question please press star 1.

As a reminder today's conference is being recorded, if you have any objections you may disconnect at this time.

I will now turn the meeting over to Ms. Alycia Downs. Ms. Downs, you may begin.

Alycia Downs: Hello, thank you. Good afternoon and thank you for joining us for today's COCA Conference Call entitled Overview of Bioterrorism Agents. We are very pleased to have Dr. William Bower present on this call.

We will be using a PowerPoint presentation for this call that you should be able to access on our Web site. If you have not already downloaded the presentation please go to www.emergency.cdc.gov/COCA, click on Conference Call Information Summaries and Slidesets and the PowerPoint can be found there.

Dr. Bower is a Medical Officer for the Division of Bioterrorism Preparedness and Response at the Centers for Disease Control and Prevention in Atlanta, Georgia, and he will be presenting on the call for us today.

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I will now turn the call over to Dr. Bower.

William Bower: Thank you and good afternoon to everyone out there or good morning depending on what time zone you're in. And thank you for joining. As Alycia said I'm William Bower. I'm a Medical Officer in the Division of Bioterrorism Preparedness and Response at the Centers for Disease Control and Prevention.

Today I'm going to provide an overview of bioterrorism by focusing on what are known as the Category A agents.

So next slide and then next slide so you should be at the Objectives slides. So the objectives of my talk are to identify the major biological threat agents; describe the natural transmission of the Category A biological agents and how they may differ in a bioterrorism event; to describe the clinical presentations of the Category A biological agents and describe the available treatments and prophylaxis options.

Next slide. First I will give you some of the characteristics of a bioterrorism agent or what would make a good bioterrorism agent. First is that it would have a high rate of illness among those exposed, also known as a high attack

rate. It would have a high rate of death among those who become ill or a high case fatality rate. It would have a short window between onset of illness and death, so it would have a narrow window for any treatment options.

And there would be a low level of immunity in the population, which, since we no longer vaccinate for smallpox makes it a good BT agent - at one time smallpox would not have been a good one.

Next slide. To continue with the ideal qualities, there is no effective or available treatment. Actually, most of these do have an effective treatment, but because they have a short window from onset to mortality it's really that there's not an effective treatment that can be used once you've actually identified that on the patient is infected a BT agent.

That they can be transmitted person to person; they are easy to produce and disseminate. And that they are difficult to diagnose either clinically or diagnostically and that goes back to what I said previously that actually all these are fairly easy to diagnose, but because the time that it takes to make the diagnose; it may be too late to provide effective treatment by the time that you've actually diagnosed the illness.

Next. So now we should be at the Epidemiological Clues. So now we'll show you some of the things that we look at to assess if what we see is going on is actually a bioterrorism event because some of these diseases do occur naturally, so I'm just going to give you some characteristics of what we would look for to try to sort out if this is just natural occurring disease or if it is actually a bioterrorism event.

So one would be a large outbreak with a high illness and death rate; a single case of an uncommon disease, which, smallpox would be the best example of

that because one case of smallpox anywhere in the world would be highly suspicious that it was a BT event.

That there are unusual symptoms or severity of disease. For example, a lot of the BT agents present as what appears to be community-acquired pneumonia However, if the severity of what originally looked like community-acquired pneumonia is higher than expected, it might be an indication that there's something else going on.

Infection in a non-endemic region, for example with plague - a case of plague in New Mexico would not necessarily be suspicious, however, a case of plague in say New Jersey, would be something that would make people wonder what's going on.

An unusual seasonal distribution; multiple simultaneous outbreaks in non-contiguous areas, for example, if you had three cases of anthrax spread across the country, as you saw in 2001, that would obviously be a clue that something might be going on.

And then sick and dying animals; oftentimes medical people don't necessarily think of this but the veterinarians certainly do; you could see a large die-off of animals that could mean that something had been spread in the environment and the animals may have been more susceptible to it than humans.

Next slide. So now I will present the individual agents. And this list was developed by a panel of experts who were convened to look at agents that could be used in a biological terrorism attack. The ones that are highlighted will be reviewed in this presentation.

These pathogens have been identified as likely agents for use as biological weapons based on their potential for mass number of casualties, ability to produce a lethal illness, requiring prolonged and extensive care, a short incubation period and contagious potential and their ability to produce non-specific symptoms that mimic endemic infectious diseases and complicate the diagnostic process.

Now inclusion of these as Category A agents was based on public health impact and delivery potential to large populations; it was not based on their availability or technical expertise needed to use. If it were based on availability then smallpox would fall way off this list.

Next slide. So you should be on the first Anthrax slide. Anthrax is found commonly among grazing animals such as cattle, sheep and goats. Humans get infected naturally with anthrax in the US usually by coming into contact with infected animals or animal products.

There are three forms of anthrax disease, which are cutaneous, inhalational and gastrointestinal.

Next slide. Anthrax is contracted through contact with the reservoir, which are infected animals and the soil. Cutaneous anthrax is the most common type and is acquired through direct contact with spores that enter the skin through a cut or scrape. This is commonly scene in people who butcher animals or those that handle hides or skins of animals that have been contaminated with anthrax spores.

Some of you all may have been familiar with the cases that occurred recently in Pennsylvania and - or when I say recently in the last two years,

Pennsylvania and Connecticut both were related to people who were making drums and using animal skins from Africa to make the drum heads.

Outbreaks of cutaneous anthrax have also occurred by transmission from fly bites. If meat from an animal with anthrax infection is eaten people can get the gastrointestinal form of the disease. And if the bacteria germinate in the throat it will cause the oropharyngeal form, which you can see there in the picture is a picture of oropharyngeal disease.

And if spores of anthrax are inhaled the spores can germinate in the lymph nodes of the mediastynum causing a pulmonary or mediastinal anthrax infection.

Next. Cutaneous anthrax accounts for more than 80% of all naturally acquired cases. Once a person has been exposed to the anthrax spores through a break in the skin there is an incubation period that ranges from 1-12 days depending on the size of the inoculum.

After the incubation period a papule will form that will break down into an ulcer after one to three days. The ulcer may have surrounding vesicles. Over approximately four days this ulcer will form a painless eschar that gradually heals over a week or longer. Most cases of cutaneous anthrax recover; however, approximately 20% progress to a systemic form of the disease.

That rate, however, drops to less than 1% if treated with antibiotics. However, antibiotics do not change the progression of the lesion.

Next slide. Inhalational anthrax occurs when spores are inhaled. The incubation period is usually only two to three days but can range up to 60 days if spore germination is delayed.

Initial symptoms can be non-specific such as malaise, low-grade fever, non-productive cough, sore throat with absence of rhinorrhea or, drenching sweats, a prominence of dyspnea and chest pain and an absence of grossly purulent sputum.

Next slide. One of the hallmarks of pulmonary anthrax is evidence of mediastinal widening and pleural effusions. Once inhaled the spores are taken up by macrophages and brought to the closest lymph nodes, in this case those in the mediastynum.

There the spores germinate and cause a hemorrhagic process in the lymph nodes, which can be seen by chest x-ray and CT scan as widening of the mediastynum. This is pathognomonic for mediastinal anthrax and if seen on x-ray with the symptoms previously discussed, should be considered anthrax and reported immediately. Pleural effusion is also quite common in pulmonary anthrax.

Next slide. With any form of systemic anthrax disease, which includes pulmonary, gastrointestinal, oropharyngeal or septic, intravenous antibiotics should be used. Ciprofloxacin or doxycycline, or both in combination, are recommended for treatment of both adults and children.

In addition one or two antimicrobial agents that have good activity against anthrax such as imipenem, clindamycin, rifampin, or a macrolide should also be used in conjunction. Penicillin can be used in conjunction with other antibiotics but should never be used alone because anthrax has an inducible beta-lactamase that can inhibit the activity in the penicillin class of antibiotics.

At least 50% of systemic cases will have concurrent meningitis so at least one of the antibiotics used should have good CSF penetration.

Supportive care is also important and patients may need airway management and care for fluid volume levels and shock. In the anthrax cases in 2001 drainage of pleural fluid in pulmonary cases appeared to improve the outcome.

Anthrax Immune Globulin, or AIG, is a recently developed product that can be used to neutralize anthrax toxin. It has been used in one case of inhalational anthrax and appeared to be beneficial. The key to its use is to use it early in the course of the disease before the patient becomes critically ill.

So if you think that you have a case of inhalational anthrax it would be good to talk with the CDC about the case where we have SMEs or Subject Matter Experts that can help you decide if Anthrax Immune Globulin would be beneficial. Also the CDC is the only place that you can get that product.

Next slide. Post-exposure prophylaxis for anthrax is with 60 days of antibiotics in conjunction with anthrax vaccine in a three-dose regiment at zero, two and four weeks. The antibiotics provide immediate prophylaxis and should be given even if vaccine is not immediately available.

Unlike for treatment, penicillins can be used alone as prophylaxis if the strain is known to be sensitive to penicillins. Just of note, levofloxacin has recently been approved by FDA for use as post-exposure prophylaxis in pediatric patients after exposure to aerosolized anthrax.

The vaccine is added because there is a potential risk in persons exposed to aerosolized anthrax spores for the spores to remain present in the lungs and germinate after a course of antibiotic prophylaxis is completed.

Next slide. So now you should be on the first Smallpox slide. Smallpox is caused by Variola virus. There are two forms of Variola virus: Variola major and Variola minor. There are four clinical presentations of smallpox. Ordinary smallpox makes up the vast majority and I will describe its presentation over the next few slides.

The other variants of the disease are hemorrhagic, flat, and modified. These are very difficult to recognize unless you are in the midst of an outbreak. Hemorrhagic and flat smallpox have extremely high fatality rates approaching 100%. Modified smallpox occurs in persons with partial immunity from previous vaccinations and present as a febrile illness without rash.

Smallpox is spread via respiratory droplets or aerosol expelled from the oropharynx. It may also be spread by direct contact, making contact with infected bed linens and clothes a risk factor for infection. Only a small number of virions or viral particles are believed to be an infectious dose, approximately 10 to 100 virions.

Approximately 30% of persons exposed to smallpox go on to develop the disease, and of those approximately 30% will die.

Next slide. Now I will go over the clinical presentation - or characteristics of smallpox. Smallpox has a febrile syndrome and the important point here is that the fever will occur one to four days prior to the rash. And there is a classic smallpox lesion, if you go to the next slide.

Since the last case of smallpox in the US was in 1949 many clinicians are unfamiliar with the disease and the disease is most likely to be confused with chickenpox. This slide shows the difference in lesions between smallpox and chickenpox.

For smallpox all the lesions are in the same stage of development; you can see on the left. And they're deep-seated lesions, they're described as like a BB under the skin - feeling like there's a BB under the skin - whereas chickenpox, which most of you all have probably seen, the rash will be in different stages of development.

As you can see there are some lesions that are drying up while other new lesions developing. And the skin over the vesicle is very thin; it's just a thin wall vesicle.

So next slide. The distribution of the lesions is, in smallpox, is also different than chickenpox. If you go to the next slide you can see the difference in the distribution patterns of smallpox and chickenpox. Smallpox tends to affect the head and the extremities more so, and chickenpox lesions are generally more dense on the trunk.

Next slide. And the last characteristic is that, as you probably know, smallpox is one of the few infectious diseases that you will have lesions on the palms and soles.

Next slide. So this slide shows the normal progression of smallpox. Following the exposures there's an incubation period ranging from 7-19 days. Then the patient enters the prodromal phase of two to four days where there is an abrupt onset of influenza-like symptoms that include a fever greater than 38.3

degrees Centigrade, malaise, myalgias, headache, nausea, vomiting, backache and the patient will appear very sick.

However, the patient is not infectious to others during the prodromal phase. The next phase is the early rash phase. The rash usually begins in the mucosal membranes of the mouth as small red spots on the tongue and back of the throat. These lesions enlarge and ulcerate allowing the virus to shed when the patient coughs.

The early rash phase normally precedes the visible skin rash by about 24 hours meaning the patient is infectious to others before visible symptoms are evident. The rash phase begins around the time the lesions in the mouth break down and lasts about 21 days. The rash phase stages are shown in the last text box of this slide and will be further explained on the next slide.

The next slide, the rash first appears as papules although they differ somewhat in size, they all have a similar appearance. By Day 5 the fluid in the vesicles has become cloudy and looks like pus. At this stage the pox are called pustules. At this time the fever usually rises and the patient feels quite ill.

On Day 7 the rash is definitely pustular, note that the pox, although varying somewhat in size, all resemble each other in appearance. The rash is now so characteristic that there should be no mistaking the diagnosis.

Gradually the pustules dry up and dark scabs form. The scabs begin to appear between 10 and 14 days after the rash first develops. The scabs contain live virus and until all scabs have fallen off the patient may be infectious to others. By Day 20 the scabs have usually fallen off and light colored pigmented areas of skin are observed.

Over a period of weeks the skin gradually returns to its normal appearance, however, scars, which last for life, may remain.

Next slide: Smallpox Medical Management. Identification and vaccination of contacts is used to prevent disease. Once contacts are identified they are quarantined and watched for symptoms of illness. If symptoms develop isolation is used to prevent transmission.

Currently there is no specific medical treatment for smallpox other than supportive care. However, there are two antivirals Cidofovir, which is currently available and a drug under development called ST246, which is available as an investigational new drug.

Both of these drugs have activity against orthopox viruses; however, since these drugs were developed after the last natural occurring case of smallpox they've never been tested in a case of smallpox, but believe that they would treat the illness.

Next slide: so Smallpox Prevention and Control. Spread most often occurs by face to face contact. All contacts of cases and contacts of contacts of cases are vaccinated. This ring vaccination strategy was used to eliminate naturally occurring smallpox. This strategy works because vaccination can prevent or at least lessen the severity of disease if vaccination occurs within four days of exposure.

In addition to the ring vaccination strategy, however, mass vaccination may be necessary because of the potential for reoccurring attacks and/or public demand for vaccination.

Next slide. Dryvax, the smallpox vaccine used to eliminate naturally occurring smallpox has been replaced by a new product called ACAM2000. ACAM2000 is a live vaccinia virus vaccine just like Dryvax. The only difference is that ACAM2000 is harvested from tissue culture cells, whereas Dryvax was harvested from calf lymph.

ACAM 2000 was developed after naturally occurring smallpox was eradicated and there is very limited human experience with ACAM2000 but since it is based on essentially the same virus stock that was used for Dryvax it is believed that it will be as good at preventing smallpox as Dryvax.

Immunity is good for about five years if vaccinated once but protection wanes over about 10 years and since the majority of smallpox vaccinations ended in the early 1970s most of the US populations is not considered immune. However having been vaccinated in the past may reduce morbidity and mortality to some extent.

Next slide. So we should be on the first Plague slide. Plague is an infectious disease of animals and humans caused by a gram negative nonsporulating bacterium called *Yersinia pestis*. People usually get plague from being bitten by a rodent flea that is carrying the plague bacterium or while handling an infected animal.

Millions of people in Europe died from plague in the Middle Ages when human homes and places of business - or work were inhabited by flea-infested rats. Today modern antibiotics are effective against plague but if an infected person is not treated promptly the disease is likely to cause illness or death.

Next slide. There are three types of plague: Bubonic plague results from an infection in the lymph node causing a large swelling of the lymph node,

scepticemic plague occurs when the bacteria enter the bloodstream, and pneumonic plague occurs when the bacteria infect the lungs. Each is described in more detail on the next slides.

Next. *Yersinia pestis* is most commonly transmitted between animal reservoirs to humans via bites of infected fleas. Primary bubonic plague is transmitted from animal reservoirs to humans via bites from flea vectors as indicated in Line A or bites or scratches from infected animals or direct contact with infected animal carcasses as in Line B.

Primary scepticemic plague is defined as systemic *Yersinia pestis* infection but without apparent preceding lymph node involvement. This can occur from bites from flea vectors as in Line A or bites, scratches or contact with infected animals or carcasses, again Line B.

Primary pneumonic plague is naturally acquired from the inhalation of respiratory droplets from infected animals such as cats, as in Line C. *Yersinia pestis* used in an aerosol attack would present the pneumonic form of plague as well.

Secondary bubonic and scepticemic plague cases may occur via person to person transmission that results from contact with infected sputum or fluid from buboes as in Line D. Secondary pneumonic plague occurs from the inhalation of respiratory droplets from a person with pneumonic plague as in Line C.

Next slide. Next I will describe the clinical presentation of pneumonic plague. After inhalation the incubation period is usually one to six days. The initial onset of the disease involves non-specific signs and symptoms including the acute onset of fever, chills, malaise and myalgias associated with progressive

lethargy, associated chest pain and increasing dyspnea and a productive cough of copious watery mucoid sputum that may also be bloody.

Without treatment the disease rapidly progresses to adult respiratory distress syndrome or ARDS characterized by refractive pulmonary edema. Signs of shock including hypertension and eventual organ failure may also occur. Without early detection and treatment in less than 24 hours pneumonic plague is almost universally fatal.

Next slide. If you suspect a case of plague it is important to start treatment immediately to prevent systemic disease. Traditionally streptomycin, tetracycline or doxycycline have been used for the treatment of plague, however, gentamicin is considered the drug of choice.

Gentamicin and ciprofloxacin are not currently approved by the FDA for treatment of plague and must be used under an IND regulation if you're getting them from the CDC; obviously if this occurs in your hospital you are able to use gentamicin off label.

Supportive care of patients is also critical including fluid management and hemodynamic monitoring. Many patients will require intensive care with respiratory support owing to complications of gram negative sepsis. In mass casualty situations where the medical care delivery system is not able to meet the demands of patient care oral antibiotics may need to be substituted for intravenous antibiotics for the treatment of patients with plague.

The possibility of a *Yersinia pestis* strain resistant to conventional antibiotic therapy is of concern and should be considered particularly if the patient deteriorates despite early initiation of appropriate antibiotic therapy. CDC recommends initiating treatment with two drugs believed to be effective

against *Yersinia pestis* until anti-microbial susceptibility data is available from the isolate.

Next slide. Prophylaxis for plague is with oral doxycycline or ciprofloxacin for seven days following last contact with a patient who has plague or from whatever the exposure could be if it was an intentional release of plague.

There is - some of you may know that - or have heard that there was a plague vaccine; however, it is no longer manufactured and it was only protective against bubonic plague and not the pneumonic form.

Next slide. So now you should be on the first Botulism slide. Botulinum toxin is the most lethal neurotoxin known and is colorless, odorless and tasteless. The lethal dose for humans is approximately one nanogram per kilogram.

There are seven types of botulinum toxin designated Types A through G. Types A, B, E and F cause natural disease in humans while types C, D and G rarely cause disease in humans but rather cause natural disease in birds, horses and cattle.

Type A is primarily found in North America, Type B is primarily in Europe and Type C is typically found in seafood and water environments.

Next slide. *C. botulinum*, the bacterium that produces botulinum toxin, can be found in soils, lake sediments, marine sediments and in the guts of many animals. It is transmitted to humans when food becomes contaminated, a wound becomes contaminated, or when the intestinal tract of infants and adults become colonized.

The mode of transmission denotes the clinical form of botulism (i.e. foodborne, wound, or intestinal), however the clinical presentation is the same regardless of the mode of transmission.

A terrorist attack could take the form of food or beverage contamination with botulinum toxin or an aerosolization and inhalation of botulinum toxin.

Next slide. The time from exposure to clinical manifestation varies for each form of botulism. For wound botulism the incubation period is 4 to 14 days; for inhalational botulism the incubation period is 24 to 72 hours, and for foodborne botulism the incubation period is typically 18 to 36 hours but can range from two hours to eight days.

The length of incubation is directly related to the amount of toxin the individual is exposed to. The disease generally begins with evidence of cranial nerve dysfunction often including blurry vision, diplopia, ptosis, expressionaless facies, regurgitation and dysarthria/dysphagia and then progresses to muscle weakness with a characteristic descending flaccid paralysis.

Next slide. The mainstay of therapy is rapid administration of botulinum antitoxin and meticulous intensive care including careful monitoring of respiratory function and provision for mechanical ventilation when needed. Paralysis and ventilator dependency may last for weeks to months.

Aminoglycoside antibiotics are contraindicated for treatment of secondary infections since they can exacerbate the neuromuscular blockade.

Next slide. Rapid administration of antitoxin is very important and should be given to patients as soon as a diagnosis of botulism is suspected since

confirmation can take several days and the antitoxin is most effective if given within 24 hours of the onset of symptoms.

A heptavalent antitoxin is available and should be administered if the type of botulism toxin is unknown. Hypersensitivity reactions are known to occur in some patients; therefore if possible skin testing should be performed on all patients before they receive antitoxin. Antitoxin prevents progression of paralysis by binding free circulating toxin but will not reverse the paralysis already present.

Next slide. So now you should be on the first Viral Hemorrhagic Fever slide. The hemorrhagic fever viruses are in fact a diverse group within the envelope single stranded RNA viruses consisting of members of four separate viral families.

Members of the family Filoviridae are Ebola and Marburg viruses; the etiologic agents of severe hemorrhagic fever with high mortalities. The Arenaviridaes include the viruses causing Lassa Fever, Argentine Hemorrhagic Fever and Bolivian Hemorrhagic Fever.

Within the family Bunyaviridae are the Crimean-Congo Hemorrhagic Fever virus and a number of the hantaviruses that cause hemorrhagic fever with renal syndrome. And finally the family Flaviviridae contains the most common cause of viral hemorrhagic fever, Dengue virus and Yellow Fever virus.

Next slide. The hemorrhagic fever viruses possess many qualities considered desirable for a biological weapon. Study animals and accidental laboratory infection in humans document that most hemorrhagic fever viruses are highly infectious in aerosol form. They also tend to have a low infectious dose, have

a high morbidity and mortality, have few effective medical counter measures and have the propensity to cause public fear and panic in the presence of outbreaks.

Next slide. The incubation period for viral hemorrhagic fevers varies. Persons are not infectious during the incubation period. In general, the clinical features of viral hemorrhagic fevers can be divided into two phases, early and late. Early manifestations are non-specific but a positive tourniquet test may provide a diagnostic clue.

Hemorrhagic manifestations occur later in the course of illness and are often accompanied by hypertension, shock, renal failure and capillary leak. Clinical clues include ecchymosis, petechiae, bleeding from nose, gums or puncture sights and GI bleeding.

Next slide. Continuous findings in viral hemorrhagic fevers range from flushing to small discrete petechiae to large ecchymotic lesions. These findings vary by severity of disease and by causative virus.

Next slide. Specific therapies exist for a minority of the viral hemorrhagic fevers. The antiviral nucleoside analog ribavirin can be effective in the treatment of viral hemorrhagic fevers due to the bunyaviruses and arenaviruses. It substantially reduces mortality in cases of hemorrhagic fever renal syndrome from hantaviruses and is thought to reduce mortality in Crimean-Congo Hemorrhagic Fever as well. However the intravenous form of ribavirin is not readily available.

Intensive care support can improve outcome. Aggressive fluid management algorithms using simple clinical parameters such as blood pressure and hemotocrit have greatly reduced mortality in Dengue Hemorrhagic Fevers and

may be effective in other viral hemorrhagic fevers. Respiratory isolation should be used to prevent transmission to healthcare workers.

Next. So here are a few sources of information on bioterrorism agents and the CDC also provides some information on emergency preparedness for BT agents. And that concludes this review so I'll be happy to answer any questions.

Coordinator: At this time...

Alycia Downs: Yeah, now we can open up the lines for the question and answer session.

Coordinator: Okay, at this time we are ready to begin the question and answer session. If you would like to ask a question please press star 1, please unmute your line and record your first and last name when prompted; to withdraw your request please press star 2. One moment please.

Okay, our first question, your line is open.

Question: Thank you for taking my call. I primarily work in training private military contractors that go overseas and so forth. Is there any information that you know of in terms of what type of bioterrorism attacks would be most likely within the continental United States?

William Bower: Now all I can say is that the agents that I went over all have - are considered to have the same likelihood.

Question cont'd: I see.

William Bower: There's probably some people that have more classified information on that; that have some intelligence information that may lead you one way or the other but that changes from month to month. So basically what I've been told is that all the Category A agents are considered one as likely as another.

Question cont'd: I see.

William Bower: But then, I mean, you do have to take in into account that the organism that cause anthrax and plague are readily available; that you could go out and find those anywhere whereas smallpox it would be hard to find smallpox except in some clandestine freezer where they didn't destroy it back in the late 70s or early 80s when the WHO requested that.

Question cont'd: I also read an article about a year ago about the ease with which botulinum toxin can be manufactured; is that considered an agent that is very easy for terrorists to manufacture?

William Bower: I believe so, yes.

Question cont'd: Great. Well that answers my questions. It's a tremendous improvement in my knowledge in these fields and I thank you very much for your time.

William Bower: Thank you.

Coordinator: Your next question; your line is open.

Question: Thank you. Are you aware of any Dengue Fever in the continental United States, in the Southeast or Southwest or along the Gulf Coast? As I saw in Spanish language newspaper suggesting that it was in Mexico and Central America.

William Bower: Well, you know, I don't work in the Dengue Fever branch.

Question cont'd: Okay.

William Bower: But I do believe that there have been some cases along the Texas-Mexican border. And my understanding is that they don't know if they were contracted in Mexico and then they came across into the US or they were acquired in the US. That's my limited knowledge on Dengue and the continental United States.

Question cont'd: Well you answered my question verifying that just wasn't crazy rumor and there might be something to that. I am surgeon for the Mississippi State Guard, not the National Guard, but State Guard, and one of the things that we're trying to get up and running is about terrorist response, first response, that kind of thing so that's very helpful. Thank you.

William Bower: You're welcome.

Coordinator: Our next question comes; your line is open.

Question: Thank you. I was curious about the botulism antitoxin. What happens if it's administered and it turns out not to be botulism?

William Bower: Well I don't think anything.

Question cont'd: Okay, so there's no adverse side effects?

William Bower: Right, it's an immunoglobulin so it would just be like when they used to give immunoglobulin before you traveled several years ago. I mean, the only

potential risk that you could have is that it's horse serum; I think it's produced from horses so you could have a reaction to some of the proteins in horse serum and that's why they recommend that you do sensitivity testing before that.

But short of having any anaphylactic response to the horse serum, just getting the antibodies wouldn't cause you any problem.

Question cont'd: Okay, that was going to be my follow-up question about contraindications.

William Bower: Yeah, the contraindications would be that you know that you are allergic to equine products.

Question cont'd: Thank you.

William Bower: Or that you've had a previous reaction. I mean, obviously if you had a previous reaction then you wouldn't want to receive it, although you can desensitize someone.

Now I'm not familiar enough with it to know that if - likely I would venture to say that if you know that you'd been exposed to botulism toxin and you were having some of the classic features of botulinum toxin that even if you had had a reaction previously that they would try to desensitize you and still give it to you.

Question cont'd: So is that sort of a progressive administration?

William Bower: Yes, yes.

Question cont'd: Okay.

William Bower: There's a whole protocol on how to desensitize someone.

Question cont'd: Okay.

Coordinator: Okay, our next question, your line is open.

Question cont'd: Thank you very much, Dr. Bower. My question comes to you from your slide number twelve where you show the image of the classic mediastinal widening.

William Bower: Okay.

Question cont'd: And I would like to know if any Ameritrax cases where you mentioned that there was quite a bit of pleural effusion; did that pleural effusion change the radiograph significantly where you would not recognize that mediastinal widening?

Or does that mediastinal widening take quite a long time to develop, where if we had a terrorist event where quite a lot of anthrax is dumped on a population would we actually see that mediastinal widening or would we see probably death first?

William Bower: Well I think that you would see the mediastinal widening. I mean, when someone comes in ill with a respiratory symptom one of the first things that they do would be get a chest x-ray. Because the lymph nodes in the mediastynum are swollen because of the anthrax multiplying within the lymph nodes that would be one of the first things you would see on a chest X-ray. In the 2001 attacks, 70% of the first 10 cases reported presented with mediastinal widening on CXR but all presented with some abnormal CXR findings.

Question cont'd: So how long does that take to happen, two days? Ten days?

William Bower: It would...

Question cont'd: Post exposure...

William Bower: Right, it would be two to three days. I mean, that would be one of the first things that you would start seeing.

Question cont'd: So that pleural effusion wouldn't confuse the picture?

William Bower: I don't think so, no.

Question cont'd: Okay. And did - were there very many cases of cutaneous anthrax during the Amerithrax episode?

William Bower: What...

Question cont'd: Do we know?

William Bower: Right, there were a total of 17 people who were ill.

Question cont'd: Yes.

William Bower: And I think about half of them had cutaneous but I don't know the exact number. But there were - probably about half of them had cutaneous anthrax.

Question cont'd: Okay. And can you speak to us a little bit more about smallpox as a bio-weapon? You didn't go into very many details of how that would look if it were weaponized.

William Bower: Well I...

Question cont'd: We've heard of smallpox being antibiotic and vaccine resistant or mixed with other agents? Do you - can you tell us if it would be - if the weaponized smallpox might be the hemorrhagic maybe or the flat? Do we have any knowledge of that?

William Bower: Well, the flat or the hemorrhagic is not a characteristic of the virus itself. It's believed to be the body's immune response that there is - somehow the people who have flat or hemorrhagic smallpox your body is actually responding to it differently.

But as far as manipulating the smallpox virus I'm not privy to any information on that nor have I seen anything that would indicate that that would be something that would be highly likely. I mean, anything is possible but, the - weaponizing smallpox would be harder than weaponizing some of the other agents that I've described.

And so that's all I know about the weaponizing of smallpox.

Question cont'd: All right, thank you very much; we appreciate this presentation.

William Bower: Thank you.

Coordinator: Your next question, your line is open.

Question: Thank you, Dr. Bower. My questions concerns like powder exposures and the patient treatment. I was wondering if you could describe what should - should

prophylaxis begin immediately or only after lab confirmation of that environmental sample?

William Bower: Well since you have an incubation period of at least 24 hours but most likely two to three days, I think that you could wait on confirmation because response teams now have rapid test kits in the field, but also each state lab I'm pretty sure can test for anthrax and have a response within 24 hours.

Question cont'd: Right. In our state our field tests are not being regarded as being valid because of the variation etcetera. So what we are trying to teach our first responders and police etcetera are to use the state LRN laboratory as a confirmatory laboratory.

William Bower: I believe that that would be the best course of action.

Question cont'd: Okay, so wait until the confirmation of the environmental to prophylax?

William Bower: Yeah, I believe because you should be able to get...

Question cont'd: That within - yes...

William Bower: ...within 24 hours.

Question cont'd: ...24 hours. Very good. Thank you, Dr. Bower.

Coordinator: Your next question, your line is open.

Question: Thank you for taking my call. You mentioned a tourniquet test with viral hemorrhagic fever, so what is that?

William Bower: Basically you just take like a blood pressure cuff and pump it up and I don't know the specifics like for how long you do it, but you just pump it up for maybe 5 or 10 minutes and then when you release it you'll just see little petechiae where the cuff was. And that's just indicating the fragileness of the capillaries, that's the virus is causing the vessel walls to break down.

Question cont'd: Got it. Thank you.

William Bower: You're welcome.

Alycia Downs: Dr. Bower, I want to thank you for providing our listeners with this information. And I want to thank our participants for joining us today.

In case you didn't get a chance to ask a question please send an email to coca@cdc.gov that's C-O-C-A@CDC.gov. The recording of this call and the transcript will be posted to the COCA Web site at www.emergency.cdc.gov/coca as they come to us.

You have a year to obtain Continuing Education credits for this call. All Continuing Education credits for COCA conference calls are issued online through the CDC Training and Continuing Education online system, www2a.cdc.gov/tceonline.

Thanks again, Dr. Bower. And I hope everyone has a wonderful day.

Coordinator: Thank you for participating in today's conference call. You may disconnect at this time.

END