

**Centers for Disease Control and Prevention
Clinician Briefing, Monkeypox
Conference Call, June 13, 2003
Summary of Call**

***Please note: Data and analysis discussed in these presentations were current when presented. Data collection and analysis are ongoing in many cases, therefore updates may be forthcoming elsewhere on this website, through publications such as [CDC's Morbidity and Mortality Weekly Report](#) or other venues. Presentations themselves will not be updated. Please bear this in mind when citing data from these presentations*

OVERVIEW OF THE MONKEYPOX OUTBREAK

Dr. Joanne Cono
Medical Epidemiologist
Co-Lead of Monkeypox Epidemiology and Surveillance Team

As you know, the CDC and a number of affected states are conducting a multistate investigation of the monkeypox outbreak. CDC first became involved last Wednesday when we received notification of the outbreak from the Wisconsin State Health Department. I and another medical epidemiologist traveled to Wisconsin to assist in the investigation where we visited some patients that had been hospitalized with a febrile rash illness. The next day CDC identified a monkeypox-like virus in specimens taken from these patients. This virus was confirmed on Sunday thereby identifying the first outbreak of monkeypox ever to occur in the United States.

To date, four states are involved in the outbreak for a total of 81 cases under investigation, with 34 in Indiana, 26 in Wisconsin, 19 in Illinois, and 2 in Ohio. Thus far cases have essentially involved a mild to moderate type illness consisting of prodrome of a febrile illness that includes respiratory systems, significant lymphadenopathy, and sore throat. There has also been some rhinorrhea, backache, and headache noted. These symptoms are followed by development of a rash that progresses through stages of vesiculation, pustulation, and umbilication and then goes on to scab over. Some of the early lesions on these patients have been ulcerated. These lesions are usually distributed over the head, trunk, and the extremities, and satellite lesions develop on the palm, soles, and extremities. These rashes can be quite generalized, and there is some variability in them from patient to patient.

So far, all of the infected patients have had contact with some animal implicated in this outbreak. As I'm sure you are aware, this has been the prairie dog. We believe that these prairie dogs were in contact with some Gambian giant rats that were imported from Ghana. These rats have been collected, and testing for monkeypox infection is in progress at CDC.

INFECTION CONTROL

Dr. Chesley Richards
Co-Leader, CDC Clinical and Infection Control Team for Monkeypox

The CDC posted interim guidance on infection control and exposure management on its Web site last Sunday evening. I want to emphasize that these are interim recommendations. As we learn more about this U.S. outbreak and more about monkeypox, these guidelines may be changed and updated.

Infection control guidance recognizes that we believe that the vast majority of cases thus far have resulted from animal to human transmission; however, person-to-person transmission certainly can occur. There have been some cases reported in the media where person-to-person transmission was suspected, but I want to emphasize that these cases are still under investigation, and we are not sure yet that they represent bonafide person-to-person transmission. Nevertheless, in our guidance we have implemented recommendations for the use of standard contact and airborne precautions to minimize the risk of person-to-person transmission.

I refer you to the CDC Web site where we have posted interim infection control and exposure management guidelines, which include our recommendations for general precautions for infection control. For health care settings we are recommending hand hygiene after all contact with infected patients and the environment of care, the use of gown and gloves for contact with patients or their environment of care, eye protection, and respiratory protection including a NIOSH-certified N95 respirator. Patients should be placed in negative pressure rooms for airborne isolation precautions. The guidance also includes recommendations regarding disinfection and the disposal of contaminated waste.

The Web site also offers guidance for outpatient management of persons who are suspected of having monkeypox infection. In general, we recommend that such persons be segregated from other patients, preferably in a private room with negative pressure. This type of room may exist in emergency departments but may not be available in other outpatient settings. A surgical mask should be placed over the patient's nose and mouth as soon as he or she arrives at the site of care. Our guidance emphasizes that patients, and public health authorities when they are involved, should alert clinicians whenever possible that a patient suspected of infection with monkeypox is coming into an outpatient facility for care so that proper precautions can be taken.

Our guidance includes recommendations for monitoring of exposed health care personnel. In general, exposed personnel who are not symptomatic need to have enhanced surveillance for symptoms for a period of 21 days after their exposure. This would include measuring their temperature at least twice daily during that time and also monitoring for other symptoms that may represent monkeypox. I want to emphasize that health care workers who are caring for monkeypox patients should adhere to infection control precautions and be vigilant for fever and other symptoms even if they have had smallpox vaccination in the past.

In terms of home management of patients who are either not sick enough to be admitted to a health care facility or who are discharged to home after a period of hospitalization, we recommend home isolation precautions. Our guidance for home isolation includes management of hand hygiene, laundry, contaminated dishes and eating utensils, and contaminated surfaces. We currently recommend that isolation precautions be continued until all lesions are crusted. Again, for asymptomatic contacts we recommend a 21-day period during of enhanced surveillance for symptoms such as fever, sore throat, cough, or skin rash.

SPECIMEN COLLECTION

Dr. Joanne Cono

There are a number of specimens that may be collected to assist in diagnosing a case of monkeypox. Laboratory diagnosis is a part of the criteria for confirming a case along with the clinical criteria of the typical rash along with other symptoms of temperature, headache, backache, lymphadenopathy, sore throat, cough, and shortness of breath, as well as the epidemiologic criteria of being in contact with one of the implicated animals or someone who is ill who has been in touch with one of the implicated animals.

Specimen collection guidelines have been newly positioned on the CDC monkeypox Web site. There are detailed but very pragmatic instructions about what specimens a clinician should collect based on the patient's presentation. Diagnosis is currently being made by PCR analysis and viral culture. Serology also can be helpful in moving further through the diagnostic chain.

Specimens are taken from the actual rash by unroofing a lesion and collecting fluid from it. Biopsy specimens from skin are helpful as well as sera or whole-blood specimens. We have found that a throat swab has been helpful in persons who have had an epidemiologic link to a patient but have not yet manifested the rash and have some of the prodromal symptoms, such as sore throat. Extensive details are available on the CDC Web site.

Dr. Chesley Richards

One other thing to emphasize is that if specimens are going to be taken from a potential monkeypox patient in clinical settings, it is critical that that be done in communication and conjunction with local and state health departments.

GUIDANCE ON USE OF SMALLPOX VACCINE

Dr. Walter Orenstein

Director, National Immunization Program

I'm going to talk about the rationale for use of smallpox vaccine to control monkeypox and other orthopoxviruses. Then, Louisa Chapmen from the National Immunization Program will go over the actual recommendations. As a preamble, I think it's important to say that we have very limited experience in the United States with regard to monkeypox, so a lot of our rationale is derived from experience in African outbreaks.

First, monkeypox can be a serious disease. Studies have shown different death-to-case ratios ranging from 1 to 33%. Most of the African studies have had a 4 to 10% mortality rate. In this U.S. outbreak, a substantial number of persons with suspected monkeypox have been hospitalized. In fact, today's MMWR reported that 26% of the cases were hospitalized, although it is not clear how sick the patients were. We certainly have seen a substantial number of hospitalizations. So clearly this disease is worth preventing.

The second point is that smallpox vaccine administered pre-exposure is highly effective. In almost all studies, the effectiveness of a dose prior to exposure is 85% or higher, and in a number of the studies more than 90% effective. That cross-reaction from the vaccinia virus induces cross-protection to another orthopoxvirus, monkeypox.

A third issue, particularly when we begin to talk about post-exposure, is that the incubation period for monkeypox is generally similar to the incubation period for smallpox,

about 7 to 17 days with an average of about 12 days. What this means is that if post-exposure vaccination is effective against smallpox, then reasoning by analogy, the assumption is that post-exposure vaccination would be effective against monkeypox. There are several lines of evidence for the effectiveness of smallpox vaccine against smallpox post-exposure. These include the fact that when you give it by vaccination, you bypass replication in the respiratory tract, which usually takes several days, and antibody response is detectable early, about 10 days after vaccination and before the normal onset of illness following exposure for smallpox. Cell-mediated immunity also may be induced early in the incubation period to prevent or modify illness. There is also epidemiologic evidence showing that early vaccinations are associated with amelioration, and there is softer evidence, but nevertheless evidence, showing that it can be associated with complete prevention of illness, although for neither prevention or modification of illness is the evidence absolute.

The next concern is the risk of transmission. We do not really know what the animal-to-human transmission risk is, but there are also concerns about human-to-human transmission of monkeypox virus. Many of the studies looking at household transmission have had rates around 7%, some as high as 15% or more. If you look at non-household transmission through more casual types of contacts, the rates have generally been on the order of one to three percent. So there can be a small but definite risk of transmission of the virus from human to human. The risk from animals is not, as I said, clear.

Based on the experience of the 1960s, the risk of death associated with smallpox vaccination was about one to two deaths per million doses administered. To put this risk in perspective, we need to look at the minimum and maximum risk for both household and non-household contacts of monkeypox. If we assume that for household contacts the minimal risk would be a 7% transmission rate and a 1% death-to-case ratio, we arrive at a risk of 7 deaths per 10,000 cases of exposures to monkeypox. If the risk of transmission were 15% and the death-to-case ratio 10%, then the risk of death becomes 150 deaths per 10,000 exposures in the household setting. This compares with 1 to 2 deaths per million resulting from smallpox vaccination. Looking at non-household monkeypox contacts, the risk of death ranges from 1 to 45 per 10,000, lower than that for household contacts and substantially lower than the perceived risk of death associated with smallpox vaccination.

Another issue is that for instances of intimate exposure we have removed most of our contraindications for vaccination, including vaccinating children as young as one year of age. The data show that, in general, the rates of serious reactions in children under age one are not significantly different from the adverse reaction rates for primary smallpox vaccination in adults. The big concern has been the risk of post-vaccination encephalitis, which was 42 per million in a 1968 10-state survey. This translates to .4 per 10,000, still well below the potential risks of death that might occur from monkeypox itself.

In developing the recommendations for use of smallpox vaccine, we concluded that the vaccine is effective against monkeypox, that for persons with intimate contact with an infected person or animal the benefits of vaccination exceed the risk, and that vaccination post-exposure is likely to be effective.

RECOMMENDATIONS FOR USE OF SMALLPOX VACCINE FOR EXPOSURE TO MONKEYPOX

Dr. Louisa Chapman
Medical Officer on detail to Smallpox Vaccine Adverse Events Monitoring and Response
Activity
CDC

There are some general aspects that are relevant to all CDC recommendations. These recommendations were developed with an attempt to balance the risk of smallpox vaccination against the risks of monkeypox exposure. Dr. Orenstein has just gone through some of the data upon which that balance was based. Because there is little direct data, the guidance is heavily reliant on expert judgment.

It is recommended that people vaccinated in the monkeypox setting be followed the same way we currently recommend for persons in response teams in the pre-event smallpox setting, including following people to ascertain take rates, to revaccinate when major reactions are not identified, and to monitor for adverse events.

It is important to try to get laboratory confirmation of suspected cases of monkeypox. This needs to be done in laboratories with the appropriate skill and bio-safety standards, and these labs should also be able to look at monkeypox, varicella, and vaccinia as well as other relevant viruses. It is particularly important to confirm that monkeypox is the source of the infection when directly exposed people for whom vaccination would be recommended are people who have contraindications to smallpox vaccination in the pre-event smallpox setting. In that situation, it's particularly important to get urgent laboratory confirmation before vaccinating those contacts.

In general this guidance refers to close contact. In the smallpox setting, greater than three hours of direct exposure within six feet has been accepted as general guidance for close contact. That was felt to be reasonable for the monkeypox setting as well. When we talk about intimate contact that was defined as direct exposure to body fluids or lesions of affected persons or animals. Judgment must be applied. There will be people who do not strictly meet these criteria but who might be candidates for vaccination, particularly when exposures occur in health care settings, child care settings, and so on. We encourage people to consult with their state and local health departments in making judgments about vaccination in this setting.

Following are some questions we have received about use of smallpox vaccination for monkeypox with responses reflecting CDC guidance.

Question 1:

Should persons investigating suspected human or animal monkeypox cases, including [veterinary and animal control personnel](#), receive smallpox vaccination? If so, should a prior history of recent vaccination with a confirmed take be required or is it acceptable to vaccinate these people as they depart for the investigation?

Answer:

Ideally, investigators should have previously received the smallpox vaccination within the past three years, and a take should have been confirmed. When this is not possible and for more recent vaccinations, the vaccine site should have at least crusted over before the investigator leaves for the investigation. But if neither of these is feasible, it is appropriate to vaccinate investigators as they depart for the field. Investigators who currently or previously have been

involved in field investigations and exposed to persons or animals infected with monkeypox but who have not previously been vaccinated should be vaccinated as soon as possible, preferably within four days of their initial direct exposure.

Any investigator who has an active vaccination site that has not yet healed should follow the site care precautions currently advised for health care workers vaccinated in the pre-event smallpox vaccination setting. This is important to prevent contact transfer among individuals, but also to prevent potential contamination of field samples in the investigation. Field investigators, even if vaccinated, should continue to observe the recommended standard, contact, and airborne infection control precautions including, when appropriate, the use of N-95 respirators. The guidance published on the CDC Web site mentioned previously can be consulted for more specific details.

Question 2:

Should health care workers who care for suspected cases of monkeypox be vaccinated?

Answer:

Previously or currently exposed health care workers should be vaccinated within the initial four days of direct exposure, but vaccination should also be considered for people who are within two weeks of their most recent exposure to a monkeypox case. Vaccination should occur as soon as possible after confirmed exposure. The vaccine site should be managed as recommended for health care workers in the pre-event smallpox vaccination guidance.

Health care workers selected to care for monkeypox patients should, ideally, not have any of the contraindications to smallpox vaccination in the pre-event smallpox vaccination setting. Priorities should be given to using health care workers who were previously vaccinated and who had confirmed takes to care for these monkeypox patients. However, when necessary, health care workers may be vaccinated immediately prior to beginning their clinical care duties. Again, the vaccine site should be managed as recommended for health care workers in the pre-event vaccination program.

Health care workers should continue to observe the recommended standard, contact, and airborne infection control precautions even if vaccinated.

Question 3:

Should smallpox vaccination be recommended for contacts of human monkeypox cases? If so, how is contact defined, e.g., family, classroom, and so on? And, what is the recommended interval for vaccination following exposure?

Answer:

Close contacts, defined as household contacts, and others who have had close or intimate contact with human monkeypox cases after the case became symptomatic and who are within four days of their initial direct exposure should be vaccinated. Vaccination also should be considered for persons who are within two weeks of their most recent exposure.

As general guidance, close contact has been defined as greater than three hours of direct exposure within six feet of a monkeypox-infected person, and intimate contact refers to contact resulting in exposure to body fluids or lesions of the affected persons. However, judgment must be applied to determine the significance of contact in individual exposure settings. State and

local health departments should be consulted regarding decisions about vaccination of contacts who may not strictly meet these criteria, particularly in exposures that occur in childcare, school, or health care settings.

Question 4

Is smallpox vaccination recommended for persons who've been exposed to a recently acquired healthy prairie dog or other small mammals from implicated distributors?

Answer

At present, smallpox vaccination is recommended only for persons who have, within the past four days, had direct physical contact with sick prairie dogs acquired since April 15 within the affected areas. Vaccination should also be considered for persons with similar contact within the past two weeks. In addition, vaccination may be considered for persons who have within the past two weeks had close contact likely to have resulted in exposure to this environmentally hearty virus through respiratory secretions or through fomites on contaminated surfaces.

As general guidance, close contact is being defined as greater than or equal to three hours of direct exposure within six feet, and this is reasonable guidance for assessing persons who may have had fomite exposure in veterinary settings. Again, such persons should be vaccinated within four days of initial direct exposure if possible. Vaccination sites for persons involved in veterinary care settings should be managed as advised for health care workers in the pre-event smallpox program. Veterinary health care workers should observe the same infection control practices recommended for human health care workers, which specifically includes standard, contact, and airborne infection control precautions including use of personal protective equipment, currently an N-95 respirator, when appropriate even if vaccinated.

Question 5

What contraindications to smallpox vaccination should be observed for persons exposed to monkeypox infection?

Answer:

For health care workers, household contacts, and other close or intimate contacts who have been exposed within the past two weeks to a symptomatic human or animal confirmed to have been infected with monkeypox, but who have contra-indications to smallpox vaccine receipt in the pre-event smallpox setting, the nature of the exposure needs to be very carefully assessed. The risk of monkeypox disease for persons intimately exposed to symptomatic monkeypox cases is believed to be greater than the risk of adverse events resulting from vaccinia exposure for most persons for whom smallpox vaccination would otherwise be contraindicated in the pre-event smallpox setting.

In persons with close or intimate exposure within the past two weeks to a person or animal symptomatic with a laboratory confirmed monkeypox infection, neither age, pregnancy, nor history of eczema are contraindications for smallpox vaccination. Current active eczematous disease is more of a concern, but in instances when the potential vaccinee has had true close or intimate exposure to confirmed monkeypox infection, the risk of contracting monkeypox would still likely be greater than the risk of complications with smallpox vaccination, and vaccination would be recommended.

Smallpox vaccination is still contraindicated for persons who have severe immunodeficiency and T-cell function deficits. This includes HIV-infected adults with CD4 lymphocyte counts less than 200 (or the age equivalent count for HIV infected children), solid organ and bone marrow transplant recipients or others currently receiving high dose immunosuppressive therapy, and persons with lymphosarcoma, hematologic malignancies, or primary T-cell congenital immunodeficiency. These persons have a risk of severe complications from smallpox vaccination that may approach or exceed the risk of disease from monkeypox exposure. Consultation with your state and local health departments and CDC is recommended regarding judgments about whether such persons should be vaccinated post exposure.

With the exceptions of the persons with severe T-cell function deficits outlined above, health care workers and others intimately exposed to humans or animals symptomatic with laboratory confirmed monkeypox infection within the past four days should receive smallpox vaccination. Vaccination should also be considered for such persons within two weeks of the most recent exposure. If there are any difficulties in obtaining rapid laboratory confirmation for these situations, the state health department should be urgently consulted.

Precautions to prevent the spread of vaccinia from the vaccination site are particularly important when children are vaccinated. The vaccination site should be managed as recommended for health care workers in the pre-event vaccination program. Persons who care for recently vaccinated children should be vigilant to observe the recommended standard and contact infection control precautions with regard to the vaccination site.

Question 6

What is the role of cidofovir and vaccinia immune globulin (VIG) in treatment and prophylaxis of these cases?

Answers

No data exist to directly inform the appropriate use of either VIG or cidofovir for prophylaxis or treatment of monkeypox. The currently available information is that smallpox vaccination is the preferred prevention measure for exposed persons. VIG has not been demonstrated to be effective in treatment or prophylaxis in monkeypox. cidofovir has significant toxicity and should be considered only for treatment of life-threatening monkeypox infection, not for prophylactic use.

Question 6

Should pre-exposure smallpox vaccination be offered to veterinarians, veterinary staff, and animal control officers in the affected regions of affected states?

Pre-exposure smallpox vaccination is not recommended for unexposed veterinarians, veterinary staff, or animal control officers in the affected states. Routine use of appropriate standard contact and airborne infection control measures is stressed. The exception is persons who may be involved in field investigations who should be vaccinated as recommended under the first question.

Dr. Walter Orenstein

I would like to make two additional points. One is to remind everyone that the use of smallpox vaccine in the monkeypox setting is considered an off-label use and requires an IND. Second, with regard to smallpox liability and compensation issues, if health care workers who are vaccinated become members of smallpox response teams, they are protected both in liability and potential compensation issues. Others, such as monkeypox response teams, would have to have their usual kinds of protection. There is no special program for that.

QUESTIONS AND ANSWERS

John Hanifan
Oregon Health Science University

In the index family in Wisconsin, a cat scratch was involved. How sure are you that the cat is not carrying this?

Dr. Joanne Cono

I'm afraid that at this time I don't have further information about the cat. The state of Wisconsin's Department of Health has been extensively involved in the investigation there, and I'm sure there is additional information available. Unfortunately, I don't have it to share.

Peggy Nell
IDSA

Could you please go over the two items you just spoke to at the end regarding off-label use and liability protections, because I'm trying to envision a setting in which clinically there are the desirable subcategories for vaccination. I now need to kind of re-walk those scenarios according to whether it's an individual who is exposed to a sick person, an animal health care worker or not or field investigator or not, etc. So, can you just run back through that?

Dr. Walter Orenstein

The first thing is that use of the vaccine in this setting is considered off-label use, so the state health departments have been given a special consent form for use. Since this is not truly a bioterrorist smallpox preparedness vaccination, from a theoretical perspective it doesn't fall into the liability protection or the compensation provisions of existing law. However, if the health care workers, in particular, do this and become members of smallpox response teams, then there may be a way to cover them. I'm not a lawyer and I don't think there's a lawyer on the phone, but clearly this is not a bioterrorism use, and that's what the legislation covers.

Peggy Nell

Right. But, given my track record it's Friday afternoon, so probably by the time I get off this phone, there's somebody with monkeypox in my hallway. Are you saying that the health departments already have these special consent forms?

Dr. Walter Orenstein

Yes. The health departments have the special consent forms. The IND has been approved. They have the vaccine from their pre-event program. So, if you want to vaccinate anybody, you should be able to get the forms from your health department.