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CDC HEALTH ADVISORY

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Interim Centers for Disease Control and Prevention (CDC) guidance for use of smallpox vaccine, cidofovir, and vaccinia immune globulin (VIG) for prevention and treatment in the setting of an outbreak monkeypox infections:

The following guidance on the use of smallpox vaccine, cidofovir, and vaccinia immune globulin (VIG) is provided by CDC for purposes of monkeypox outbreak control. In most instances, only limited data are available on which to directly base recommendations and thus the guidance is primarily based on expert opinion. This interim CDC guidance was developed using the best available information about the benefits and risks of smallpox vaccination, VIG, and cidofovir for prevention and/or management of smallpox, monkeypox and complications of vaccinia infection. Smallpox vaccine for controlling outbreaks of monkeypox would be available under an investigational new drug (IND) protocol sponsored by CDC.

Limited information is available on efficacy of smallpox vaccination for prevention of monkeypox. The data suggest that pre-exposure smallpox vaccination is highly effective (≥85%) in protecting persons exposed to monkeypox from disease (1-5). No information is available on the efficacy of post-exposure vaccination. Data which suggest smallpox vaccination following exposure to smallpox is effective in preventing or ameliorating disease suggest that post-exposure smallpox vaccination should have similar impact against monkeypox. Data from investigations in Africa in the 1980's suggested that in household settings, secondary transmission occurred to about 8 – 15% of contacts. Among infected human cases, reported mortality rates have ranged from 1 – 33%, but were most frequently reported to be between 4-10% (1-8).

Because of the seriousness of this disease, CDC has developed interim guidance which attempts to balance the risks of smallpox vaccination against the risks posed by exposure to monkeypox infection. This interim guidance will be re-evaluated as more information becomes available.

It is important that vaccinators actively follow vaccinees, evaluate vaccination sites for major reactions, and re-vaccinate when takes are not identified, as currently occurs in the pre-event smallpox vaccination program. State and local health departments should provide information on how vaccinees should seek consultation on evaluation of vaccination sites for major reactions or for potential complications of vaccination.

Rash illnesses suspected to be monkeypox should be confirmed by laboratory evaluation which, in addition to determining the presence of monkeypox, should have the capability to detect varicella, vaccinia and other relevant viruses. Confirming suspected cases of monkeypox is particularly important before recommending vaccination in instances where there is close or intimate contact between persons with rash illness and persons with contraindications to smallpox vaccination in the pre-event smallpox vaccination setting such as pregnant women, persons with eczema, and similar persons at higher risk for life-threatening complications of vaccinia exposure. As general guidance, for purposes of smallpox exposure, close contact has been defined as ≥3 hours of direct exposure within 6 feet and this is reasonable guidance for monkeypox exposure as well. Intimate contact refers to contact resulting in exposure to body fluids or lesions of affected persons. However, judgment must

be applied to determine the significance of contact in individual exposures situations. If there are difficulties in obtaining rapid laboratory confirmation in these situations, the state health department should be urgently consulted.

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

Ideally investigators of suspected or confirmed monkeypox cases should have received smallpox vaccination within the past 1-3 years. When possible, priority should be given to using investigators, veterinarians, and animal control personnel who previously were vaccinated and who had a confirmed take. Ideally the vaccination site should have crusted over before deployment. However, if this is not feasible these individuals may be vaccinated immediately before deploying for the field investigation. Unvaccinated investigators currently involved in field investigations or who have been recently involved in such work should be vaccinated as soon as possible, preferably within 4 days from initial direct exposure. Any investigator with an active vaccination site that is not healed should follow the precautions advised for health care workers (HCWs) with regard to the vaccination site care to avoid potential contamination of field samples or of transmission of vaccinia to others (9).

Field investigators of suspected cases of monkeypox should observe recommended standard, contact, and air-borne infection control precautions even if vaccinated. These include the use of recommended personal protection equipment (currently N95 respirator) when appropriate (10).

2 - Should HCWs who care for suspected cases of monkeypox be vaccinated?

A. Previously or currently exposed HCWs

HCWs currently caring for suspected or proven monkeypox cases or who have been recently involved in such care should be vaccinated. Vaccination is recommended for persons who are within 4 days of initial direct exposure and should be considered for persons who are within 2 weeks of most recent exposure. Vaccination should occur as soon as possible after confirmed exposure. Vaccination sites should be managed as recommended for HCWs in the pre-event smallpox vaccination program (9).

B. HCWs who may be asked to care for monkeypox patients in the future

Ideally, HCWs selected to care for suspected monkeypox cases should not have any of the contraindications to smallpox vaccination in the pre-event smallpox vaccination setting (11, 12). When possible, priority should be given to having HCWs who were previously vaccinated, with confirmed takes, care for patients with suspected monkeypox. When such workers are unavailable, HCWs may be vaccinated immediately prior to beginning their clinical care duties. Vaccination sites should be managed as recommended for HCWs in the pre-event vaccination program (9).

HCWs who care for suspected cases of monkeypox should continue to observe recommended standard, contact, and air-borne infection control precautions including use of personal protective equipment (currently N95 respirator) (10) when appropriate, even if vaccinated.

C. Clinical laboratory workers

Interim guidance on appropriate handling of routine clinical laboratory specimens from persons suspected or confirmed to be infected with monkeypox is under development and will be released shortly.

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

Close contacts, defined as household contacts as well as others who have had close or intimate contact with human cases after the case became symptomatic, and who are within 4 days of initial direct exposure to a monkeypox case should be vaccinated. Vaccination should be considered for persons who are within 2 weeks of most recent exposure. As general guidance, for purposes of smallpox exposure, close contact has been defined as ≥3 hours of direct exposure within 6 feet and this is reasonable guidance for monkeypox exposure as well. Intimate contact refers to contact resulting in exposure to body fluids or lesions of affected persons. However, judgment must be applied to determine the significance of contact in individual exposures situations. State and local health departments should be consulted regarding decisions about vaccination of contacts, and in particular be consulted for contacts who may not meet the strict definitions of close or intimate contact above, especially in child care, school, or health care settings.

4 - Should smallpox vaccination be recommended for persons who have been exposed to a recently acquired healthy prairie dog or other small mammals from implicated distributors?

Smallpox vaccination should be recommended only for persons who have, within the past 4 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 such contact within the past 2 weeks. In addition, vaccination can be considered for persons who have, within the past 2 weeks, had close contact likely to have resulted in exposure to this environmentally hardy virus in respiratory secretions or through fomites on contaminated surfaces. As general guidance, for purposes of smallpox exposure, close contact has been defined as ≥3 hours of direct exposure within 6 feet and this is reasonable guidance for monkeypox exposure in veterinary settings as well. Such persons should be vaccinated within 4 days of initial direct exposure if possible. These recommendations may change should evidence show that other symptomatic small mammals pose significant risk.

For persons involved in investigations or veterinary care settings, vaccination site care should be managed as recommended for HCWs (9).

Veterinary health care workers should observe the same infection control practices recommended for human HCWs. Specifically, veterinary care workers who care for suspected cases of monkeypox should continue to observe recommended standard, contact, and air-borne infection control precautions including use of personal protective equipment (currently N95 respirator) (10) when appropriate, even if vaccinated.

Interim guidance on appropriate handling of routine clinical laboratory specimens from animals suspected or confirmed to be infected with monkeypox is under development and will be released shortly.

5 - What contraindications to smallpox vaccination should be observed for persons exposed to monkeypox infections?

For HCWs, household, close or intimate contacts who have been exposed within the past 2 weeks to a symptomatic human or animal confirmed to be infected with monkeypox but who have contraindications to smallpox vaccine receipt in the pre-event smallpox setting (11, 12), the nature of exposure should be assessed carefully. If there are difficulties in obtaining rapid laboratory confirmation in these situations, the state health department should be urgently consulted. 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 be otherwise contraindicated

in the pre-event smallpox vaccination setting. In persons with close or intimate exposure within the past 2 weeks to a person or animal symptomatic with laboratory confirmed monkeypox infection, neither age, pregnancy, nor a history of eczema are contraindications to receipt of smallpox vaccination. Active eczematous disease is more concerning, but in instances when the potential vaccinee has had true close or intimate exposure, the risk of contracting monkeypox would likely still be greater than the risk of complications of smallpox vaccination.

Smallpox vaccination is still contraindicated for persons who have severe immunodeficiency in T-cell function, defined as:

- HIV-infected adults with CD4 lymphocyte count less than 200 (or age appropriate equivalent counts for HIV infected children);

- solid organ or bone marrow transplant recipients or others currently receiving high dose immunosuppressive therapy (i.e. 2 mg/kg body weight or a total of 20 mg/day of prednisone or equivalent for persons whose weight is > 10 kg, when administered for $\geq$ 2 weeks); and

- persons with lymphosarcoma, hematological malignancies, or primary T-cell congenital immunodeficiencies.

These persons may have a risk of severe complications from smallpox vaccination that may approach or exceed the risk of disease from monkeypox exposure. Consultation with state and local health departments and CDC should be sought regarding judgments about vaccination of such persons in the post-exposure setting.

With the exception of persons detailed in the preceding paragraph, HCWs and others intimately exposed to humans or other animals symptomatic with laboratory confirmed monkeypox infection within the past 4 days should receive smallpox vaccination. Vaccination should be considered for such persons within 2 weeks of most recent exposure. If there are difficulties in obtaining rapid laboratory confirmation in these situations, the state health department should be urgently consulted.

Precautions to prevent spread from the vaccination site are particularly important when children are vaccinated. Vaccination sites should be managed as recommended for HCWs in the pre-event smallpox vaccination program (9). Persons who care for recently vaccinated children should be vigilant to observe recommended standard and contact infection control precautions with the vaccination site.

6 - What is the role of cidofovir and VIG in treatment and prophylaxis of these cases?

No data exist to directly inform the appropriateness of use of either VIG or cidofovir for prophylaxis or treatment of monkeypox. With the currently available information, smallpox vaccination is the preferred prevention measure recommended for exposed persons.

VIG has not been demonstrated to be effective in treatment or prophylaxis of monkeypox.

Cidofovir has significant toxicity and should only be considered for treatment of life-threatening monkeypox infections, not for prophylactic use.

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

At this time pre-exposure smallpox vaccination is not recommended for unexposed veterinarians, veterinary staff, and animal control officers in the affected areas, but routine use of appropriate standard, contact and air-borne infection control measures

should be stressed. The exception is persons who may be involved in field investigations, who should be vaccinated in advance (see question 1). This recommendation will be re-evaluated as more information becomes available.

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10. Interim Infection Control and Exposure Management Guidance in the Health-Care and Community Setting for Patients with Possible Monkeypox Virus Infection: http://www.cdc.gov/ncidod/monkeypox/infectioncontrol.htm

Monkeypox Infections In Animals: Interim Guidance for Veterinarians and Pet Owners: http://www.cdc.gov/ncidod/monkeypox/animalguidance.htm

11. CDC. Smallpox Vaccination and adverse reactions: Guide for clinicians. MMWR 2003; 52 (RR-4); 1-28. (see also website: http://www.bt.cdc.gov/agent/smallpox/vaccination/contraindications-public.asp .)

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DEPARTMENT OF HEALTH AND HUMAN SERVICES