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*Monkeypox Technical Background and Outbreak Implications
for Bioterrorism Preparedness*

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Abstract. Monkeypox, a viral disease related to smallpox, has appeared in humans in the Midwest. Although officials do not believe that this outbreak is bioterrorism, the delay between the initial presentation of an unusual disease and the notification to the federal government has raised concerns regarding the state of bioterrorism preparedness. Possible issues related to this outbreak include the regulatory process that allowed import of diseased animals; how efficient the public health system response has been in alerting the government to potential health emergencies; and whether the monkeypox outbreak provides an opportunity to evaluate recent efforts to increase public health preparedness and the state of bioterrorism preparedness.

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Monkeypox: Technical Background and Outbreak Implications for Bioterrorism Preparedness

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Summary

Monkeypox, a viral disease related to smallpox, has appeared in humans in the Midwest. Though monkeypox usually has a fatality rate of 1 to 10%, no fatalities have occurred in the outbreak, which has been linked to pet rodents. Although officials do not believe that this outbreak is bioterrorism, the delay between the initial presentation of an unusual disease and the notification to the federal government has raised concerns regarding the state of bioterrorism preparedness. The Centers for Disease Control and Prevention (CDC) have provided guidance to local communities regarding handling of ill patients and animals, treatment regimens, and sample protocols. The CDC have recommended and released smallpox vaccine as prophylaxis against monkeypox infection. The CDC and the Food and Drug Administration banned interstate commerce in prairie dogs and certain other rodents and the CDC suspended import of all rodents from Africa. Possible issues related to this outbreak include the regulatory process that allowed import of diseased animals; how efficient the public health system response has been in alerting the government to potential health emergencies; and whether the monkeypox outbreak provides an opportunity to evaluate recent efforts to increase public health preparedness and the state of bioterrorism preparedness. This report will be updated as events warrant.

Introduction

An outbreak of monkeypox, a disease caused by a virus closely related to smallpox virus, began in May 2003 in Wisconsin. As of this writing, 79 suspected and diagnosed

cases have been identified in multiple states.¹ Most of the afflicted individuals were infected by ill, pet prairie dogs. Officials do not believe that the current outbreak was caused by an act of terrorism.² This report describes previous human outbreaks, symptoms, and treatments of monkeypox; the government response to the current outbreak; and implications this outbreak may have in evaluating the public health system response to biological terrorism.

What Is Monkeypox?

Monkeypox's causative agent is an Orthopox virus in the Poxviridae family. In the wild, rodents, predominantly squirrels in central and western Africa, are the reservoir for this virus. Monkeypox is a zoonotic disease, meaning that humans can catch the disease from infected animals. Human monkeypox outbreaks occur infrequently and generally in rural, African rainforest villages. The largest recent confirmed outbreak occurred in the Democratic Republic of Congo in 1996–1997, with 88 cases over a 12-month period.³ Between January 2000 and March 2002, 22 cases of monkeypox worldwide were reported to the World Health Organization.⁴ Monkeypox is not native to North America and has not previously been diagnosed in the United States.

Human monkeypox symptoms are similar to those of smallpox. Initial symptoms include fever, aches, and malaise. Unlike smallpox, monkeypox often causes swollen lymph nodes. These symptoms are followed by a rash which converts into blisters. An incubation period of up to 2 weeks is possible, and symptoms may last for 2 to 4 weeks.⁵

There is no known, proven cure for monkeypox. Monkeypox victims are treated with supportive care. There are indications that some antivirals, namely cidofovir and ribavirin, may be effective. Cidofovir has been recommended for treating monkeypox during this outbreak, but only in life-threatening cases, due to its significant side effects.⁶ Because monkeypox is closely related to smallpox, the smallpox vaccine (vaccinia) is an effective prophylactic. Vaccination with vaccinia is estimated to provide greater than 85% protection against monkeypox.⁷ Vaccinia may reduce the severity of a monkeypox infection if the victim is vaccinated a few days after exposure to monkeypox, generally before symptoms appear.

¹ Daily updates of the number and location of suspected monkeypox cases are provided by the CDC online at [<http://www.cdc.gov/od/oc/media/monkeypx.htm>].

² Linda Spice, "13 Sick After Prairie Dog Contact; Milwaukee Pet Store Employee, Two Others Remain Hospitalized," *Milwaukee Journal Sentinel*, June 6, 2003.

³ Y.J.F. Hutin, R.J. Williams, P. Malfait, *et al.*, "Outbreak of Human Monkeypox, Democratic Republic of Congo, 1996 to 1997," *Emerging Infectious Diseases*, 7(3) May–June 2001.

⁴ J.G. Breman, I. Arita, and F. Fenner, "Preventing the Return of Smallpox," *New England Journal of Medicine*, 348(5), 463-466, January 30, 2003.

⁵ CDC, "What You Should Know About Monkeypox - Fact Sheet," June 12, 2003.

⁶ CDC, "Interim Guidance for Use of Smallpox Vaccine, Cidofovir, & VIG for Prevention and Treatment in the Setting of Outbreak of Monkeypox Infections," June 12, 2003, available online at [<http://www.cdc.gov/ncidod/monkeypox/pdf/mphan.pdf>].

⁷ Ibid.

Monkeypox is less contagious than smallpox. Studies of African outbreaks suggest that 8-15% of those in household settings with a victim may become infected.⁸ Transmission experiments indicate that it is possible to infect others via aerosol, for example through coughing or sneezing.⁹ The human fatality rate for monkeypox is lower than that for smallpox. In documented cases in Africa, the fatality rate has ranged from 1% to 10% in unvaccinated individuals. The comparable fatality rate for smallpox is approximately 30%.¹⁰ The fatality rate in the United States may be lower than that observed in Africa because of better nutrition and health-care access.¹¹

Current Monkeypox Outbreak

The current monkeypox outbreak began in May 2003, with the onset of illnesses in Wisconsin. All cases to date have involved contact between an infected animal and the victim. The CDC investigation suggests that monkeypox entered the United States via import of infected African rodents for use as exotic pets. These rodents apparently infected nearby captive prairie dogs in a pet store. The infected prairie dogs were distributed and sold over three states. There are not any reports of wild animals in the United States becoming infected with monkeypox, although this remains a risk.

The CDC recommends that doctors follow a standard protocol when diagnosing a disease with acute, generalized rash in order to rule out smallpox.¹² If smallpox remains a possibility, physicians should alert their local and state health departments. The health departments, working with the Laboratory Response Network, can further test specimens taken from suspected cases. The health departments may then notify the CDC, which will begin an investigation and may help test the samples. In the May outbreak, physicians reportedly ruled out smallpox at an early stage because of the apparent link of the cases to ill animals.¹³ This assumption reportedly led to a 13-day delay before the local or state health departments were notified.¹⁴ Identification of the disease as monkeypox was announced by the CDC on June 7, 2003, following preliminary serologic testing and DNA analysis.¹⁵ Suspected cases of monkeypox continue to be investigated. While person-to-person transmission of the disease is possible, all diagnosed cases so far in this outbreak have been linked to animal-human transmission.

⁸ Ibid.

⁹ G.M. Zaucha, *et al.*, "The Pathology of Experimental Aerosolized Monkeypox Virus Infection in Cynomolgus Monkeys (*Macaca fascicularis*)," *Lab. Invest.*, 81, pp. 1581-1600 (2001).

¹⁰ CDC, "Basic Information About Monkeypox - Fact Sheet," June 12, 2003.

¹¹ CDC, "What You Should Know About Monkeypox ..."

¹² "The Acute, Generalized Vesicular or Pustular Rash Illness Protocol," CDC, available online at [<http://www.bt.cdc.gov/agent/smallpox/diagnosis/evalposter.asp>].

¹³ Linda Spice, "13 Sick After ..."

¹⁴ Steve Mitchell, "Monkeypox Shows Gap in Bioterror Readiness," *UPI International*, June 12, 2003.

¹⁵ CDC, "Preliminary Report: Multistate Outbreak of Monkeypox in Persons Exposed to Pet Prairie Dogs," June 9, 2003.

Government Response

In response to the outbreak, several states have banned the importation, display and sale of prairie dogs. Some state and local governments have quarantined animals or seized and destroyed them.¹⁶ Other state efforts have focused on identifying those who have been exposed to the infected animals; monitoring those who provide care for ill persons; alerting physicians to look for suspected monkeypox cases; and tracking down all of the potentially infected animals.

The CDC has banned import of all African rodents.¹⁷ The CDC and the Food and Drug Administration have prohibited the transportation, sale, distribution or release of prairie dogs and the following rodents from Africa: tree squirrels, rope squirrels, dormice, Gambian giant pouched rats, brush-tailed porcupines, and striped mice.¹⁸ The CDC suggests that states may also choose to prohibit the importation, display, and sale of other species that may carry monkeypox, such as rabbits, gerbils, or hamsters.

The CDC has issued guidelines for treatment and isolation of suspected monkeypox cases¹⁹ and guidelines for the use of smallpox vaccine to protect against monkeypox.²⁰ Smallpox vaccine is recommended for people who have had close contact with a monkeypox case. Household contacts of monkeypox cases and those who may have handled sick prairie dogs are also advised to be vaccinated. Vaccination is recommended for health care workers who are caring for known or suspected monkeypox cases or will be in the near future. All vaccinations should be done within 4 days of initial direct contact, though it may be considered for anyone with exposure within the previous 2 weeks. The CDC have recommended Vaccinia Immune Globulin (VIG), and cidofovir to counteract some of the serious side effects of the smallpox vaccine.²¹

Policy Issues

Congress has expressed interest in assuring that federal, state, and local public health organizations are held accountable for making effective use of recent funding increases to improve public health preparedness. Some policymakers have suggested that evaluating the public health response to unusual disease outbreaks may be a valuable tool for assessing improvements in public health preparedness. Others argue that unless an outbreak is categorized as a suspected bioterrorism event, it is not a true test of the nation's bioterrorism response plans. Even where a comprehensive assessment of

¹⁶ Dan Rozek and Art Golab, "Monkeypox Cases 'Will Go Up'; Dozens of Prairie Dogs Linked to Virus Can't Be Found," *Chicago Sun-Times*, June 11, 2003.

¹⁷ Authority is granted by the Public Health Service Act, 42 U.S.C. 264, see also 42 CFR 71.32(b).

¹⁸ Authority is granted by the Public Health Service Act, 42 U.S.C. 264, see also 42 CFR 70.2 and 21 CFR 1240.30.

¹⁹ Available online at [<http://www.cdc.gov/ncidod/monkeypox/infectioncontrol.htm>].

²⁰ CDC, "Interim Guidance for Use of Smallpox Vaccine ..."

²¹ For more information about the side effects of the smallpox vaccine see CRS Report RL31694 *Smallpox Vaccine Stockpile and Vaccination Policy*, by Judith A. Johnson.

bioterrorism preparedness is not possible, certain aspects of public health response are similar whether a disease outbreak occurs naturally or through an intentional act. An effective public health response includes: performing appropriate laboratory tests using protocols established through the Laboratory Response Network to rule out and/or identify the pathogenic agent; timely, accurate reporting to appropriate public health officials; rapidly disseminating accurate and consistent information to public health officials, health care providers, the media, and the public; using epidemiologic information to determine and control potential transmission vectors; and assuring appropriate medical care by rapidly providing guidelines for treatment and diagnosis.

Public health experts have favorably compared the public health system response to both SARS and monkeypox to the confused public health reaction during the anthrax attacks.²² However, some have claimed that there may still be areas for improvement, as gaps and weaknesses remain in some state and local public health communication and surveillance capabilities.²³ Development of a systematic method for using disease outbreak response to evaluate public health system preparedness could assist in identifying areas for improvement in the system and a metric for measuring improvement.

Many federal agencies regulate animal import. The regulatory situation that allows importation of diseased animals is similar to that allowing importation of invasive species.²⁴ Since many diseases are zoonotic, ill-animal importation may have bioterror implications. Such imports might be used in an agroterrorism attack by using a lightly regulated animal to introduce a disease for a different animal, causing economic harm. Another possibility might be intentionally importing and releasing ill animals to increase the number of naturally occurring fatal diseases in humans. The monkeypox outbreak is likely to increase scrutiny of these regulations and may result in new legislative proposals to modify them.

The CDC reportedly expressed concern over the delay between the occurrence of the initial case and notification of the agency.²⁵ However, in other statements, the CDC has praised the response of state officials.²⁶ Critics state that the delay between presentation and public health response suggests the notification system needs improvement.²⁷ They assert that a comparable delay in the case of smallpox would lead to a sizeable epidemic. Furthermore, simply identifying the disease as monkeypox might not rule out bioterrorism. In the early stages of this outbreak, the fact that monkeypox had never been

²² David McGlinchey, "Monkeypox Outbreak Tests Bioterrorism Response Systems," *Global Security Newswire*, June 12, 2003.

²³ General Accounting Office, *Bioterrorism: Preparedness Varied Across State and Local Jurisdictions*, GAO-03-373, April 2003.

²⁴ For a thorough review of agencies responsible for regulating importation of animals and the regulatory gaps, see CRS Report RL30123, *Invasive Non-Native Species: Background and Issues for Congress*, by M. Lynne Corn, Eugene H. Buck, Jean Rawson, Alex Segarra, and Eric Fischer.

²⁵ Chris Logan, "Feds Didn't Hear about Monkeypox for Weeks, Officials Say," *CQ Homeland Security*, June 9, 2003.

²⁶ Marilyn Marchione, "U.S. Bans Sale of Prairie Dogs; CDC Urges Smallpox Shots, But State Officials Reluctant to Comply," *Milwaukee Journal Sentinel*, June 12, 2003.

²⁷ Steve Mitchell, "Monkeypox Shows Gap ..."

previously diagnosed in the United States and had been reportedly developed as a weapon²⁸ may have raised concerns that the outbreak was not of natural origin. Following CDC notification and epidemiological investigation, the discovery of infected rodent imports from an area known to have endemic monkeypox strongly supports a natural outbreak.

Some observers have defended the delay as reasonable, since smallpox was ruled out quickly because it cannot infect animals, and there was an apparent link between the human cases and diseased animals. On the other hand, many of the diseases that have been the targets of weapons programs in the past are transferable from animal to man, such as plague, tularemia, and hantavirus.²⁹ It is conceivable that a terrorist group with access to these agents, but lacking advanced dissemination technology, would choose to use animal vectors. A documented case is the Japanese use of fleas to cause plague outbreaks in China in the 1930s.³⁰ Some critics suggest that since such links do not preclude a bioterrorism event, healthcare providers should err towards potential over-reporting.³¹

Whether the current monkeypox outbreak tests the nation's bioterror preparedness is an open question. Some claim that the early classification of this outbreak as not related to bioterrorism means that this is not a true test of the nation's bioterrorism response plans. Since this is a public health concern, the Department of Health and Human Services is the lead agency for federal response, unlike in a terror event, where the Department of Homeland Security would assume responsibility. Others claim that an outbreak of a new disease, no matter the vector, magnitude, or source, should be treated as a potential bioterror event until proven otherwise, and they suggest a need for a more rapid and coordinated response.³² Congress may consider whether to further address when and how the federal bioterror response should be engaged.

²⁸ Ken Alibek, *Biohazard: the Chilling True Story of the Largest Covert Biological Weapons Program in the World – Told From Inside by the Man Who Ran It* (New York: Random House, 1999), p. 133.

²⁹ Center for Non-proliferation Studies, Monterey Institute of International Studies, Chemical and Biological Weapons Resource page at [<http://cns.miis.edu/research/cbw/possess.htm>].

³⁰ Peter Williams and David Wallace, *Unit 731: Japan's Secret Biological Warfare in World War II* (New York: Free Press, 1989), p. 27.

³¹ Steve Mitchell, "Monkeypox Shows Gap ..."

³² Ibid.