

Transmission of Monkeypox Among Persons Exposed to Infected Prairie Dogs in Indiana in 2003

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Objective: To describe a cluster of human monkeypox cases associated with exposure to ill prairie dogs in a home child care.

Design, Setting, Participants: We identified all persons exposed to 2 pet prairie dogs in County A, Indiana; performed active surveillance for symptomatic monkeypox infection; and evaluated the types of exposure that may have resulted in infection. For children who attended the child care where the animals were housed, we also measured the rate of seroconversion to monkeypox virus.

Main Outcome Measures: Nine (13%) of 70 persons exposed to the prairie dogs reported signs and symptoms of monkeypox. Two (40%) of 5 symptomatic child care attendees reported direct contact with the prairie dogs. Two (13%) of 15 child care attendees evaluated tested positive for IgM antibodies against

orthopoxvirus; both reported symptoms consistent with monkeypox.

Results: The risk of symptomatic infection correlated with the time and intensity of animal exposure, which was 100% (4/4) among family members with extensive direct contact, 19% (5/26) among the veterinarian and nonfamily child care attendees with moderate exposure, and 0% (0/40) among school children with limited exposure ($P < .01$).

Conclusions: Monkeypox virus was transmitted from ill prairie dogs in a child care and veterinary facilities. The risk of symptomatic infection correlated with the amount of exposure to the prairie dogs. Although most cases of human monkeypox were associated with direct animal contact, other routes of transmission cannot be excluded.

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IN 2003, 72 CASES OF HUMAN MONKEYPOX were identified in 6 Midwestern states, the first cases documented in the western hemisphere.¹ The source of the US outbreak was traced to native prairie dogs (*Cynomys* species) housed at a pet distributor's facility along with wild rodents imported from Africa.² In Indiana, 16 cases of human monkeypox were identified statewide, including 9 cases in County A, Indiana, that were associated with exposure to 2 ill prairie dogs housed in a home child care facility.

The prairie dogs were purchased at a pet swap meet on May 18 and were housed at the child care facility for 11 days. On May 19, the animals were taken to 2 classes at a local elementary school. On May 24, 1 of the prairie dogs was evaluated at a veterinary office but died later that day. The second prairie dog died on May 28. The 3 family members living at the home child care facility developed a rash illness on May 29, and on June 8, the laboratory diagno-

sis of monkeypox was confirmed by the Centers for Disease Control and Prevention (Atlanta, Ga).

The risks and routes of transmission among persons exposed to monkeypox-infected animals in the United States are unknown. The objectives of this investigation were to identify cases of monkeypox among persons exposed to the 2 ill prairie dogs in County A, evaluate the types of exposure associated with monkeypox transmission, and measure the rate of seroconversion to monkeypox virus among a cohort of home child care attendees.

METHODS

SURVEILLANCE AND CASE DEFINITIONS

We obtained enrollment lists from the home child care and elementary school classes and interviewed the prairie dog owners, parents of children attending the home child care facility, parents and teachers of children attend-

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ing the elementary school, and employees at the veterinary office to identify persons exposed to the infected prairie dogs from May 18 through May 28. Exposure was defined as being in the same room with 1 or both of the ill prairie dogs. Direct contact was defined as touching, petting, or handling the animals. Exposed persons were actively monitored via telephone follow-up for signs or symptoms of possible monkeypox infection. Persons with clinical symptoms were referred to designated physicians for further evaluation, and specimens were collected for laboratory testing using methods previously described.³

Using the case definition from the Centers for Disease Control and Prevention, a suspect case was defined as a patient with fever or unexplained rash and 2 or more other symptoms (ie, chills, lymphadenopathy, headache, sore throat, cough, dyspnea, or myalgia) within 21 days of known exposure to the ill animals.⁴ A probable case was defined as a patient with fever and vesiculopustular rash within 21 days of known exposure. A confirmed case had clinically compatible illness (eg, suspect or probable case) with laboratory evidence of monkeypox infection, including monkeypox virus isolation in culture, monkeypox virus DNA by polymerase chain reaction (PCR), orthopoxvirus by electron microscopy, or orthopoxvirus antigen by immunohistochemical staining.³

Table 1. Exposure in Human Monkeypox Cases Among Persons Exposed to 2 Infected Prairie Dogs

Exposure Setting	Cases/Exposed, No. (%)
Household*†	4/4 (100)
Veterinary office‡	1/1 (100)
Home child care facility‡§	5/26 (19)
School	0/40 (0)
Total	9/70 (13)

*Three confirmed and 1 probable case. The probable-case patient was a family member who helped purchase and transport the animals but did not live in the home.

†One patient lived in the household and attended the home child care facility and is included in both groups.

‡One suspect case.

§One confirmed and 4 suspect cases.

EVALUATION OF HOME CHILD CARE COHORT

We performed a cohort study to measure the rate of seroconversion to monkeypox virus among home child care attendees and evaluated the types of exposure that may have resulted in monkeypox infection. Eligible participants included all children who attended the home child care facility during the 11 days the prairie dogs were present. After providing informed consent, the children's parents completed a questionnaire regarding demographics, home child care attendance, animal exposure, and clinical symptoms consistent with monkeypox illness. Serum specimens were collected from participants at 2 points and were evaluated for antibodies to orthopoxvirus using an IgG enzyme-linked immunosorbent assay and a newly developed IgM-capture enzyme-linked immunosorbent assay.³

RESULTS

We identified 70 persons who were exposed to the 2 pet prairie dogs, including the family associated with the home child care facility (n=4), a veterinarian (n=1), nonfamily attendees of the home child care (n=25), and children in 2 kindergarten classes (n=40) (**Table 1**). Nine (13%) of the 70 exposed persons reported signs and symptoms of monkeypox (**Table 2**). The risk of symptomatic infection correlated with the time and intensity of animal exposure: 100% (4/4) among family members with extensive direct contact, 19% (5/26) among the veterinarian and nonfamily home child care attendees with moderate exposure, and 0% (0/40) among the school children who had limited exposure (χ^2 for trend, $P < .01$).

Three family members, including a father, mother, and daughter who housed the prairie dogs in their home child care facility and have been previously reported, had laboratory evidence of disease and were classified as confirmed cases (**Table 2**).³ A fourth family member, who helped purchase and transport the animals but did not live in the home, had a vesicular rash and was classified as a probable case. The veterinarian who examined 1 of the animals and an

Table 2. Characteristics of Individuals in Human Monkeypox Cases

Case/Age, y	Status*	Exposure Setting	Exposure Dates	Onset Date	Clinical Illness	Laboratory Results
1/40	Probable	Household†	5/18	5/26	Fever, vesiculopustular rash, headache, sore throat, myalgia	IgM-, IgG+
2/8	Suspect	Child care	5/19-5/24	5/27	Fever, maculopapular rash, adenopathy, headache, cough, sore throat, myalgia	No sample
3/6	Suspect	Child care	5/19-5/24	5/28	Fever, mouth sores, adenopathy, headache, cough, sore throat, myalgia	No sample
4/6	Confirm	Child care, household	5/18-5/28	5/29	Fever, vesiculopustular rash, adenopathy, sore throat, headache, encephalitis	Culture+, PCR+, IHC+, IgM+
5/30	Confirm	Household	5/18-5/28	5/29	Fever, vesiculopustular rash, headache, sore throat	Culture+, PCR+, IHC+, IgM+, IgG+
6/33	Confirm	Household	5/18-5/28	5/29	Vesiculopustular rash, sore throat, myalgia	Culture+, PCR+, IgM+, IgG+
7/3	Suspect	Child care	5/19-5/24	6/3	Fever, papular rash with 1 pustule, sore throat	IgM+, IgG+
8/49	Suspect	Veterinary office	5/24	6/7	Fever, chills, myalgia	IgM+, IgG+
9/1	Suspect	Child care	5/19-5/24	6/9	Fever, maculopapular rash, cough, sore throat, diarrhea	PCR-, IgM-, IgG-

Abbreviations: IHC, immunohistochemical staining; PCR, polymerase chain reaction; -, negative; +, positive.

*Meets the updated interim case definitions for suspect, probable, and confirmed human cases of monkeypox (July 2, 2003).

†Family member who helped purchase and transport the animals but did not live in the home.

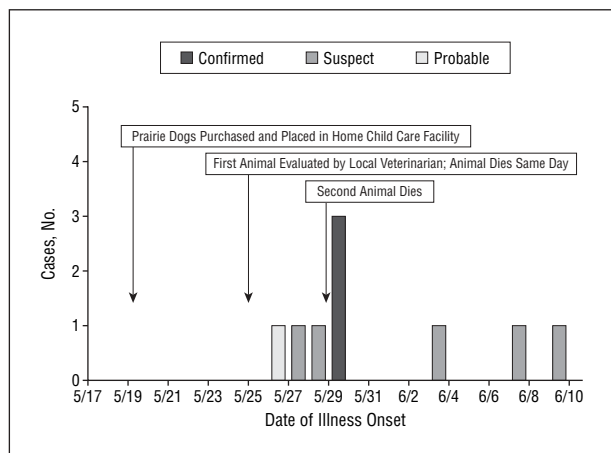


Figure. Date of onset of symptoms of human monkeypox among persons exposed to 2 infected prairie dogs in County A, Indiana, 2003.

additional 4 children who attended the home child care met the suspect-case definition. Dates of illness onset ranged from 8 to 21 days after initial exposure (**Figure**).

HOME CHILD CARE FACILITY EXPOSURE

The home child care facility was a 2-story structure of 1900 sq ft. The child care attendees spent most of their time in the living room. Once or twice a day, the children would exit the house to play in the backyard and would pass next to the cage holding the prairie dogs. At these times, some children would have direct contact with 1 or both of the prairie dogs.

Twenty-six children were identified as having attended the home child care facility while the prairie dogs were present. Of the 25 children we were able to contact, 14 (56%) were boys and 24 (96%) were white. The median age of home child care attendees was 5 years (range, 6 months to 11 years). A median of 9 children attended the home child care each day (range, 6 to 12 children per day).

Five (20%) of the 25 children contacted reported signs and symptoms of possible monkeypox, including 1 confirmed and 4 suspect-case patients (Table 2). The 6-year-old index-case patient lived in the household, attended the home child care, and had laboratory-confirmed monkeypox by culture, PCR, and immunohistochemical staining. Of the 4 children meeting the suspect-case definition, 3 (75%) had fever and maculopapular rashes. One (25%) child had fever, cough, mouth sores, and flulike illness. Of the suspect cases, only the 1-year-old had specimens collected from the rash, which was negative by PCR for monkeypox. The remaining 20 (80%) children had no signs or symptoms of febrile or rash illness.

There was no difference in home child care attendance during the prairie dog exposure period between children with symptoms (median, 6 days; range, 1-11 days) compared with children without symptoms (median, 6 days; range, 1-7 days). Two (40%) of 5 children with symptoms reported direct contact with the prairie dogs compared with 4 (20%) of 20 children without symptoms ($P=.6$) (**Table 3**). None of the child care attendees reported being bitten or scratched by the prairie dogs.

Table 3. Prairie Dog Contact Reported by Home Child Care Attendees or Their Parents by Case Status

Contact	Cases (n = 5), No. (%) [*]	No Illness (n = 20), No. (%)
Direct contact [†]		
Yes	2 (40)	4 (20)
No	2 (40)	10 (50)
Unknown	1 (20)	6 (30)
Bitten or scratched	0	0

^{*}Includes both laboratory-confirmed (n = 1) and suspect (n = 4) cases.
[†]Direct contact was defined as touching, petting, or handling the animals.

SEROLOGIC EVALUATION OF HOME CHILD CARE ATTENDEES

One or more serum specimens were obtained from 15 (60%) of 25 home child care attendees, including 3 (60%) of 5 children with symptoms and 12 (60%) of 20 children without symptoms. Eleven home child care attendees (44%) did not provide specimens for evaluation, including 2 suspect-case patients. Specimens were obtained a median of 23 days (range, 11-70 days) after last exposure to the ill prairie dogs. Two (13%) of the 15 children tested were positive for IgM antibodies against orthopoxvirus (cases 4 and 7).

One IgM-positive case was a 6-year-old girl who resided in the home where child care was provided, and she reported extensive contact with and handling of both animals. She developed fever, diffuse vesiculopustular rash, and encephalitis. The other IgM-positive child was a 3-year-old boy who attended the home child care but reported no direct contact with the animals. He developed a fever with 1 pustule and several papules on the legs. The rash resolved after about 1 week. Sera collected 15 days after his illness onset was positive for both IgM and IgG antibodies against orthopoxvirus. No other specimens were obtained for laboratory evaluation.

The 1-year-old child, classified as a suspect case who tested negative by PCR for monkeypox-virus DNA on a swab of a cutaneous lesion, had no serologic evidence of infection (case 9). All 12 children without symptoms tested negative for monkeypox antibodies.

COMMENT

Monkeypox virus is an orthopoxvirus related to smallpox and vaccinia and has been identified in numerous mammals, including rodents.⁵ Human monkeypox is a zoonotic infection that occurs sporadically in central and west Africa.⁶ Although human-to-human transmission can occur, the virus is usually acquired through direct contact with infected animals.⁶⁻⁸ In the health care setting, one study suggests transmission is likely a rare event in health care workers exposed to patients with monkeypox.⁹ The most common clinical manifestation is a febrile illness with a vesiculopustular rash.

Of the 70 persons identified as exposed to the 2 ill pet prairie dogs in County A, 9 reported symptoms of possible monkeypox. Epidemiologic and laboratory investi-

gation supports that monkeypox virus was transmitted from ill prairie dogs to persons in the household, the veterinary office, and the home child care facility, but not in the elementary school. The risk of symptomatic infection correlated with the amount of exposure to the prairie dogs.

All of the confirmed-case patients reported extensive contact with the ill prairie dogs. Based on this evidence and historical data, direct contact with the animals is the most likely mode of transmission.⁶⁻⁸ However, other potential routes of transmission such as environmental exposure or person-to-person transmission cannot be ruled out. Evidence of monkeypox virus was found by PCR in tissues, urine, and fecal specimens obtained from 1 of the 2 prairie dogs, suggesting that virus may have been shed into the environment. Further studies are needed to better define the specific routes of monkeypox transmission.

Five (19%) of 26 children exposed to the prairie dogs in the home child care facility developed symptoms consistent with monkeypox virus. However, the lack of available specimens limited the capacity to confirm all potential monkeypox cases, and laboratory evidence of infection was available for only 2 (8%) of the 26 children. There was no evidence of asymptomatic infection among the child care attendees evaluated. Although both children with laboratory evidence of infection reported symptoms consistent with monkeypox, their exposure history, clinical presentation, and illness course were very different. The intensity of exposure to the virus, as well as host immune response, may play a role in the severity of human monkeypox.

Our study had several limitations. Recall bias may have been introduced by children and parents regarding animal exposure and contact. Because not all of the exposed child care attendees had serologic studies performed, the frequency of asymptomatic infection could not be determined. Shared exposures to both animals and persons with monkeypox make it difficult to definitively attribute all human cases to zoonotic transmission. Finally, environmental sampling for the presence of viable virus on surfaces in the child care facility was not performed.

During the outbreak, the Centers for Disease Control and Prevention and the Food and Drug Administration issued an embargo on the importation of rodents from Africa.¹⁰ The agencies also prohibited the transportation and sale or release into the environment of prairie dogs and certain species of rodents from Africa. Long-term regulations controlling the importation, quarantine, and health certification of nonnative animals should be considered. Independent of such regulation, the risks of disease transmission and injury should always be weighed carefully before wild or exotic pets are brought into a child care facility or other public settings.

A compendium by the National Association of State Public Health Veterinarians provides specific guidelines on ways to minimize the risks associated with animals in public settings.¹¹ Recommendations within the compendium include training staff and educating children about the risks of disease transmission and injury, maintaining proper hand washing and environmental disinfection, and having all animals properly screened and monitored for illnesses by a veterinarian. Application of

these recommendations may have reduced the risk of exposure to monkeypox in the home child care facility and veterinary office.

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