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Update: Multistate Outbreak of Monkeypox — Illinois, Indiana, Kansas, Missouri, Ohio, and Wisconsin, 2003

CDC and state and local health departments continue to investigate cases of monkeypox among persons who had close contact with wild or exotic mammalian pets or persons with monkeypox (*1*). This report updates epidemiologic, laboratory, and animal data for U.S. cases.

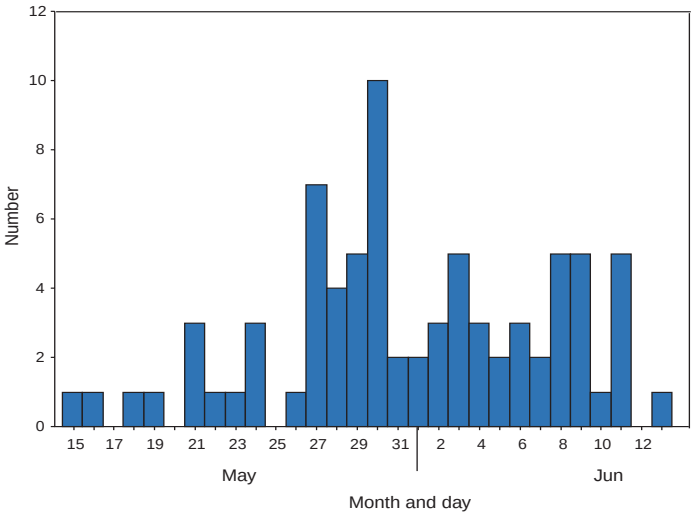
Epidemiologic investigation

As of June 18, a total of 87 cases of monkeypox have been reported to CDC from Wisconsin (n = 38), Indiana (n = 24), Illinois (n = 19), Ohio (n = 4), Kansas (n = 1), and Missouri (n = 1). Of the 87 cases, 41 (47%) were among males. The median age for the 82 patients for whom age data were available was 28 years (range:1–55 years). Data on symptom onset were available for 78 persons (Figure). Among the 75 patients for whom data were available, 20 (27%) were hospitalized. The majority of patients were not seriously ill; some were hospitalized to facilitate proper isolation.

Of the 87 monkeypox cases, 20 (23%) were laboratory confirmed at CDC (Table). Among these 20 patients, one was a child hospitalized with severe encephalitis 3 days after developing a vesicular rash, which was originally thought to be varicella-zoster virus (VZV). However, diagnostic testing for VZV and for herpes simplex virus in serum, cerebrospinal fluid, and skin lesion biopsy was negative. A skin lesion biopsy was positive for monkeypox DNA by polymerase chain reaction (PCR) and for orthopox antigens by immunohistochemical (IHC) testing.

The majority of patients had direct or close contact with wild or exotic mammals such as prairie dogs (*Cynomys* sp.). In one instance, 28 children attending a day care facility in Indiana were potentially exposed to two prairie dogs that subsequently became ill and died; 12 (43%) reported handling or petting the prairie dogs, and seven (25%) subsequently became ill with symptoms consistent with monkeypox infection. Laboratory evaluation of these children is in progress.

FIGURE. Number* of persons with monkeypox, by date of first symptom onset — Illinois, Indiana, Kansas, Missouri, Ohio, and Wisconsin, May 15–June 13, 2003



*N = 78.

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TABLE. Number and percentage of 20 laboratory-confirmed monkeypox cases, by selected characteristics — United States, 2003

Characteristic	No.	(%)
State		
Illinois	5	(25)
Indiana	6	(30)
Wisconsin	9	(45)
Age (yrs)		
6–18	7	(35)
19–48	13	(65)
Sex		
Female	8	(40)
Male	12	(60)
Clinical features		
Rash*	19	(95)
Fever	17	(85)
Respiratory symptoms†	16	(80)
Lymphadenopathy	11	(55)
Hospitalized	12	(60)
Smallpox vaccination status§	2	(15)

* For one case, rash could not be confirmed.
† Includes at least one of the following symptoms: cough, shortness of breath, sore throat, and nasal congestion.
§ Data on previous history of smallpox vaccination was available for 13 (65%) of the 20 laboratory-confirmed cases.

Laboratory Investigation

Clinical specimens obtained from 82 patients in Illinois, Indiana, Ohio, and Wisconsin were forwarded to CDC for testing. Twenty (74%) of 27 patients with skin rash-lesion specimens were laboratory confirmed for monkeypox by viral isolation, PCR, electron microscopy, and/or IHC; four were negative for monkeypox virus; one patient was found to have varicella by PCR testing; and two are pending. Two health-care workers in Wisconsin who were suspected initially of acquiring disease by human-to-human transmission had no evidence of monkeypox-specific DNA signatures in blood and nasopharyngeal and/or oropharyngeal swabs; culture results are pending. These persons did not have a rash, and IgM testing has not revealed any anti-orthopoxvirus immune reactivity.

Animal Investigation

Traceback investigations of animals are ongoing to identify how monkeypox virus was introducted into the United States. Preliminary results have determined that an animal vendor in Wisconsin (distributor A) sold prairie dogs to the index patient in Wisconsin; this vendor had obtained prairie dogs from an animal vendor in Illinois (distributor B), who had housed prairie dogs and Gambian giant rats (*Cricetomys* sp.) in close proximity. Because Gambian giant rats often are imported from regions of Africa where monkeypox is endemic,

traceback investigations of the Gambian giant rats were initiated. These investigations identified a shipment of animals from Ghana, including Gambian giant rats that were delivered to a Texas animal importer (distributor C) on April 9. Distributor C's Gambian giant rats were sold subsequently to an Iowa animal vendor on April 15 (distributor D) who in turn supplied them to distributor B. The shipment of animals from Ghana contained approximately 800 small mammals of nine different species, including six genera of African rodents that might have been the source of introduction of monkeypox. These rodent genera included rope squirrels (*Funiscuirus* sp.), tree squirrels (*Heliosciurus* sp.), Gambian giant rats, brushtail porcupines (*Atherurus* sp.), dormice (*Graphiurus* sp.), and striped mice (*Hybomys* sp.). Laboratory testing of animals from the April 9 importation from Africa is underway to determine which, if any, animals in the shipment might have introduced the virus into the United States.

On the basis of the epidemiologic link between the shipment from Ghana and distributor B, trace-forward investigations have been initiated to locate animal vendors and owners who purchased imported African rodents from the April 9 shipment or purchased prairie dogs from distributors A, B, C, and D after April 15. In addition to routine sales by animal vendors, animals also were sold or traded at "swap meets" (i.e., gatherings of animal traders, exhibitors, and buyers). An investigation of distributor B revealed that infected prairie dogs from this animal vendor might have been sold or traded at swap meets to unidentified buyers in Schaumburg, Illinois, on April 20, May 3, and May 18; Indianapolis, Indiana, on April 27 and May 18; and Columbus, Ohio, on April 19. In addition, distributor A sold infected prairie dogs at a swap meet in Wausau, Wisconsin, on May 11. In several instances, identifying individuals who purchased animals has been impossible. Invoices and other records are incomplete for many of these sales, especially those transacted at swap meets.

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Editorial Note: Preliminary findings from these investigations suggest that the primary route of monkeypox transmission to humans is from close contact with infected wild and exotic mammalian pets. Person-to-person transmission has not been identified in this outbreak. Investigations are underway to assess the possibility of secondary transmission among health-care workers and household contacts exposed to patients with laboratory-confirmed monkeypox infection.

Compared with previous reports of monkeypox among persons in central Africa (*2*), the illness associated with the current outbreak in the United States has been relatively mild. Monkeypox infection in adults has been described rarely in Africa; among adults, previous vaccination against smallpox might attenuate clinical illness (*3*). The report of encephalitis in a child indicates the potentially serious consequences of the disease.

Because suspected cases of monkeypox might actually represent varicella infections, patients should be assessed for history of varicella or having received varicella vaccine. Rash illness suspected to be monkeypox should be confirmed by laboratory evaluation, particularly if use of smallpox vaccine is being considered for purposes of monkeypox outbreak control. CDC has issued interim recommendations for use of smallpox vaccine, cidofovir, and vaccinia immune globulin (VIG) for prevention and treatment in the setting of outbreaks of monkeypox infections (*4*).

Health-care providers, veterinarians, and public health officials who suspect monkeypox in animals or humans should report such cases to their state and local health departments. CDC requests that reports of suspect cases from state health departments be directed to the CDC Emergency Operations Center, telephone 770-488-7100. Additional information about monkeypox, including a revised interim case definition (Box), is available at http://www.cdc.gov/ncidod/monkeypox.

References

1. CDC. Multistate outbreak of monkeypox—Illinois, Indiana, and Wisconsin, 2003. MMWR 2003;52:537–40.
2. Jezek ZM, Scczeniowski KM, Paluku M, Putombo M, Grab B. Human monkeypox: clinical features of 282 patients. J Infect Dis 1987;156:293–8.
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4. CDC. Interim guidance for use of smallpox vaccine, cidofovir, and VIG for prevention and treatment in the setting of an outbreak of monkeypox infections. Available at http://www.cdc.gov/ncidod/monkeypox/clinicians.htm.

BOX. Updated interim case definition for human cases of monkeypox, June 17, 2003

Clinical Criteria

- Rash (macular, papular, vesicular, or pustular; generalized or localized; discrete or confluent)
- Fever (subjective or measured temperature ≥99.3° F [≥37.4° C])
- Other signs and symptoms:
  - — Chills and/or sweats
  - — Headache
  - — Backache
  - — Lymphadenopathy
  - — Sore throat
  - — Cough
  - — Shortness of breath

Epidemiologic Criteria

- Exposure* to an exotic or wild mammalian pet† obtained on or after April 15, 2003, with clinical signs of illness (e.g., conjunctivitis, respiratory symptoms, and/or rash)

or

- Exposure to an exotic or wild mammalian pet with or without clinical signs of illness that has been in contact with either a mammalian pet§ or a human with monkeypox

or

- Exposure¶ to a suspect, probable, or confirmed human case

Laboratory Criteria

- Isolation of monkeypox virus in culture
- Demonstration of monkeypox virus DNA by polymerase chain reaction testing in a clinical specimen
- Demonstration of virus morphologically consistent with an orthopoxvirus by electron microscopy in the absence of exposure to another orthopoxvirus
- Demonstration of presence of orthopoxvirus in tissue using immunohistochemical testing methods in the absence of exposure to another orthopoxvirus

Case Classification

- Suspect case
  - — Meets one of the epidemiologic criteria

    and
  - — Fever or unexplained rash and two or more other signs or symptoms with onset of first sign or symptom ≤21 days after last exposure meeting epidemiologic criteria

- Probable case
  - — Meets one of the epidemiologic criteria

    and
  - — Fever and vesicular-pustular rash with onset of first sign or symptom ≤21 days after last exposure meeting epidemiologic criteria

- Confirmed case
  - — Meets one of the laboratory criteria

Exclusion Criteria

A case may be excluded as a suspect or probable monkeypox case if:

- An alternative diagnosis can fully explain the illness**

or

- The case was reported on the basis of contact with an ill wild or exotic mammalian pet that was subsequently determined not to have monkeypox (e.g., another etiology fully explains the illness) provided other possible epidemiologic exposure criteria are not present

or

- The case was reported on the basis of contact with wild or exotic mammalian pet with or without signs of illness that had been in contact with an ill animal or person that was determined subsequently not to have monkeypox provided other possible epidemiologic exposure criteria are not present

or

- The case was reported on the basis of contact with a person who was subsequently determined not to have monkeypox provided other possible epidemiologic exposure criteria are not present

or

- A suspect case without a rash does not develop a rash within 6 days of initial identification or examination of the case

* Includes living in a household, petting or handling, or visiting a pet holding facility (e.g., pet store, veterinary clinic, or pet distributor).
† Includes prairie dogs, Gambian giant rats, and rope squirrels. Exposure to other exotic or nonexotic mammalian pets will be considered on a case-by-case basis; assessment should include the likelihood of contact with a mammal with monkeypox and the compatibility of clinical illness with monkeypox.
§ Includes living in a household or originating from the same pet holding facility as another animal with monkeypox.
¶ Includes skin-to-skin or face-to-face contact.
** Factors that might be considered in assigning alternate diagnoses include the strength of the epidemiologic exposure criteria for monkeypox, the specificity of the diagnostic test, and the compatibility of the clinical presentation and course of illness for the alternative diagnosis.