

Monkeypox

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Etiology

Monkeypox results from infection by the monkeypox virus, an *Orthopoxvirus* related to the variola (smallpox), vaccinia, cowpox, buffalopox, and camelpox viruses. Some isolates of the monkeypox virus appear to differ in their virulence in non-human primates.

The monkeypox virus is also related to the tanapox virus, which causes Benign Epidermal Monkeypox (BEMP). The tanapox virus is antigenically unrelated to vaccinia and smallpox and does not infect New World monkeys. BEMP is characterized by epidermal pocks on the arms, face, and perineum of monkeys, without generalized illness. In humans, the tanapox virus usually causes only localized skin lesions at the site of inoculation but occasionally results in a systemic illness.

Geographic Distribution

Monkeypox was first reported in the Democratic Republic of the Congo (DRC, formerly known as Zaire) in the 1970s. This disease is currently endemic only in Central and West Africa. In 2003, an outbreak of monkeypox occurred in the Midwestern United States. The cases in the U.S. were in pet prairie dogs, other small mammals in captivity, and people who have been exposed to sick prairie dogs.

Transmission

The monkeypox virus can be transmitted to humans in bites from animals, aerosols, or by direct contact with lesions, blood, or body fluids from an infected person or animal. Most cases are zoonotic and occur after contact with an infected animal, but human-to-human transmission has also been seen. Person-to-person spread could occur as a result of skin-to-skin contact or in aerosols but it is rare and less transmissible than smallpox. The monkeypox virus can also be spread on fomites.

The route of transmission in animals is less well understood. The virus may be transmitted in aerosols, through skin abrasions, or by the ingestion of infected tissues.

Disinfection

The U.S. Centers for Disease Control and Prevention (CDC) recommends disinfection of contaminated surfaces with 0.5% sodium hypochlorite or other EPA-approved high-level disinfectants. Incineration or autoclaving is appropriate for some contaminated materials. Burial without decontamination is not recommended.

Infections in Humans

Incubation Period

In humans, the incubation period is listed by various sources as 7–17 days or 4–20 days; most infections become symptomatic after approximately 12 days.

Clinical Signs

In humans, monkeypox resembles smallpox; however, the symptoms are generally milder and, unlike smallpox, the lymph nodes are usually enlarged. The initial symptoms are flu-like and may include fever, chills, headache, sore throat, myalgia, backache, fatigue, lymphadenopathy, a nonproductive cough, and, in severe cases, dyspnea. A rash, initially characterized by macules and papules, develops 1 to 10 days later; the macules and papules develop into vesicles and pustules (“pocks”) and, in the final stage, form scabs. The skin lesions usually occur mainly on the extremities but can also be seen on the head and torso. The illness generally lasts for 2 to 4 weeks, and the skin lesions usually resolve in 14 to 21 days.

In an outbreak in the Democratic Republic of Congo, respiratory complications were seen in approximately 12% of the patients who had not been vaccinated against smallpox. One case of nonfatal encephalitis was seen in a child during the 2003 outbreak in the United States. In approximately half of all patients, hypopigmented and/or



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hyperpigmented skin lesions may be seen for up to two years. Severe scarring, as seen in smallpox, is rare.

Communicability

Monkeypox is a communicable disease in humans. Only limited human-to-human spread has been reported in the past, with estimated transmission rates of 3.3% to 30%. However, during a recent outbreak in the Democratic Republic of Congo, the transmission rate was estimated at 73%. Infected individuals may be contagious from 1 day before the rash appears and up to 21 days after the initial symptoms, or until all skin lesions have formed scabs and no other symptoms are present.

Diagnostic Tests

Monkeypox can be tentatively diagnosed if the characteristic skin lesions are present and there is a history of exposure. A definitive diagnosis can be made by isolating the monkeypox virus or by identifying orthopoxviruses in skin lesions with electron microscopy. Viruses may also be found in throat and nasopharyngeal swabs. In addition, monkeypox infections can be confirmed with polymerase chain reaction (PCR) tests or immunohistochemistry. Serology may be helpful.

Treatment and Vaccination

Treatment of monkeypox is mainly supportive. The antiretroviral drug cidofovir has been effective *in vitro* and in animal studies, but its efficacy against monkeypox in humans is unknown. The toxic effects of this drug must also be considered. The efficacy of vaccinia immune globulin (VIG) in cases of monkeypox is unknown.

The human smallpox vaccine is thought to help prevent monkeypox infections, as well as decrease the severity of the symptoms. Post-exposure vaccination may also be helpful. The CDC currently recommends smallpox vaccination only in people who have been or are likely to be exposed to monkeypox. The World Health Organization does not recommend routine vaccination of healthy people in endemic areas, as the benefits of vaccination do not appear to outweigh the risks and expense. In particular, HIV infection, with its concurrent immunosuppression, is common in the parts of Africa where monkeypox occurs.

Morbidity and Mortality

Cases of monkeypox in humans are rare and usually zoonotic. Most outbreaks in the past have been short-lived and self-limiting, with only limited person-to-person spread. Through the mid 1980s, estimates of the human-to-human transmission rates ranged from 3.3% to 30%. However, during a recent outbreak in the Democratic Republic of Congo, which continued for more than a year, the person-to-person transmission rate was estimated at 73%. Some researchers speculate that people may have become more susceptible

to monkeypox with the ending of vaccination for smallpox. The increased person-to-person transmission rate remains to be confirmed, as the outbreak occurred during a period of civil war and the study was cut short.

Estimates of the case-fatality rate for monkeypox in Africa vary from 1% to 10%, with the highest risk of death in young children. In one study of 300 patients in the Democratic Republic of Congo, the overall mortality rate was 10% and the mortality rate in unvaccinated children was 15–20%. Respiratory complications occurred in 12% of patients in this study.

During an outbreak of monkeypox in the U.S. in 2003, most cases appeared to be the result of contact with sick prairie dogs. Two of 71 patients became severely ill, one with encephalitis, and no deaths occurred.

Infections in Animals

Species Affected

Old and New World monkeys and apes, a variety of rodents (including rats, mice, squirrels, and prairie dogs) and rabbits are susceptible to infection. Approximately nine outbreaks have been documented in captive primates, mainly in rhesus macaques and cynomolgus monkeys. Infections have also been reported in langurs, baboons, chimpanzees, orangutans, marmosets, gorillas, gibbons, owl-faced monkeys (*Cercopithecus hamlyn*), and squirrel monkeys. No cases have been reported in dogs or cats to date; however, the full host range is still unknown and these and other domestic species may be susceptible. Antibodies to the monkeypox virus have been found in a wide variety of nonhuman primates, rodents, and squirrels in Africa.

The natural reservoir(s) of the monkeypox virus remains to be established but is thought to be mainly rodents. Two species of African squirrels, *Funisciurus anerythrus* and *Heliosciurus rufobrachium*, have been suggested as possible reservoirs or vectors. It is not known whether primates also maintain the infection in the wild, or are only incidental hosts.

During the 2003 outbreak in the U.S., human cases resulted from exposure to infected pet prairie dogs. An imported exotic mammal, the Gambian giant rat, was thought to have transmitted the virus to prairie dogs. The U.S. government embargoed six genera of African rodents, including rope squirrels (*Funisciurus* sp.), tree squirrels (*Heliosciurus* sp.), Gambian giant rats, brush-tail porcupines (*Atherurus* sp.), dormice (*Graphiurus* sp.), and striped mice (*Hybomys* sp.).

Incubation Period

In one study, experimentally infected cynomolgus monkeys developed symptoms 6 to 7 days after aerosol exposure to a lethal dose of virus. The CDC recommends that animals

that have been exposed to monkeypox be quarantined for six weeks after exposure.

Clinical Signs

Non-human primates

In non-human primates, monkeypox usually occurs as a self-limiting rash. The initial symptoms are a fever and 1 to 4 mm cutaneous papules, which develop into pustules then crust over. A typical monkeypox lesion has a red, necrotic, depressed center, surrounded by epidermal hyperplasia. These “pocks” can be seen over the entire body, but may be more common on the face, limbs, palms, soles, and tail. The number of lesions varies from a few individual pocks to extensive, coalescing lesions. The crusts over the pustules eventually drop off, leaving small scars. In one outbreak in common marmosets, the skin lesions persisted for 4–6 weeks.

Some animals have only skin lesions. In more severe cases, coughing, nasal discharge, dyspnea, anorexia, facial edema, oral ulcers, or lymphadenopathy may also be seen. Disseminated disease, with visceral lesions, is uncommon in natural infections. Pneumonia is common only in monkeys infected experimentally by aerosol.

Most naturally infected animals recover; however, fatalities are sometimes seen, particularly in infant monkeys. Asymptomatic infections also occur.

Rabbits and rodents

In rabbits and rodents, including prairie dogs, the initial signs may include fever, conjunctivitis, nasal discharge, cough, lymphadenopathy, anorexia, and lethargy. Animals may then develop a nodular rash, pustules (“pocks”), or patchy alopecia. Pneumonia has also been seen. Monkeypox was fatal in some but not all infected animals during the 2003 outbreak in the U.S. Mild symptoms, with no respiratory signs and limited skin lesions, were seen in an infected Gambian giant rat.

During an outbreak, veterinarians should consider the possibility of monkeypox in sick prairie dogs or Gambian rats, or any animal with a history of fever, conjunctivitis, respiratory signs, and a nodular rash.

Communicability

Monkeypox is a communicable disease in animals. Infected animals may be contagious 1 day before and up to 21 days after the initial symptoms appear, or until all skin lesions have formed scabs and no other symptoms are present. Animals can transmit the virus by direct contact or in aerosols.

Diagnostic Tests

Monkeypox can be tentatively diagnosed if the characteristic skin lesions are present, or if other symptoms consistent with the disease are seen during an outbreak. The diagnosis can be confirmed by histopathology and virus isolation. Polymerase chain reaction (PCR) tests can also detect monkeypox DNA in tissues. If the animal has not been exposed to other orthopoxviruses, virions can be detected with electron microscopy or orthopoxvirus antigens can be identified with immunohistochemistry. An ELISA test has been developed. Serology may also be helpful.

The state health department should be contacted before collecting or shipping any diagnostic samples. Serum, samples of skin lesions, and conjunctival swabs may be collected from live animals. At necropsy, tissues should be collected from all organs that have lesions. Minimally, samples of the lungs, lymph nodes, liver, spleen, kidneys, gonads, and any skin lesions should be collected. The tissues should be divided into two parts; half should be placed in 10% formalin and kept at room temperature, and the other half collected aseptically for virus isolation. Transport medium should not be used. The sample collected for virus isolation should be refrigerated if it will be shipped within 24 hours, or frozen if shipment will be delayed. **Tissues and other specimens must be packaged and shipped under secure conditions to prevent infections in humans and animals, and must comply with all local, state, and federal regulations.**

Treatment and Vaccination

Treatment is symptomatic but many animals recover spontaneously. Antiretroviral drugs have been effective in experimental infections; however, during the 2003 outbreak, the CDC recommended that all animals with suspected monkeypox be euthanized to prevent the spread of the disease.

Vaccination with vaccinia virus is protective in nonhuman primates.

Morbidity and Mortality

Sporadic cases of monkeypox occur in wild primates in Africa and approximately 9 outbreaks have been reported in captive primates. In most of these outbreaks, the morbidity rate tended to be high and the mortality rate low; respiratory disease was uncommon and most animals recovered. More severe infections were seen in cynomolgus macaques, orangutans, and infants of all species, and deaths were seen mainly in infants. Experimental aerosol infections can result in more severe disease, an increased risk of pneumonia, and higher mortality rates in adult primates.

The morbidity and mortality rates are not well documented in rodents. In prairie dogs, some infections have been fatal while other animals recovered. A single known case in a Gambian giant rat during the U.S. outbreak was very mild. Infections may be particularly common among squirrels in

Africa; many wild *Funisciurus anerythrus* and *Heliosciurus rufobrachium* squirrels have antibodies to monkeypox.

Post-Mortem Lesions [Click to view images](#)

Animals should be necropsied only by individuals who have a current smallpox vaccination, and the biological safety guidelines recommended by the CDC should be followed. [Link to CDC Interim Guidance for Necropsy and Animal Specimen Collection for Laboratory Testing (<http://www.cdc.gov/ncidod/monkeypox/necropsy.htm>)]

Due to the risk of infection, the CDC recommends that practicing veterinarians avoid doing necropsies or biopsies on suspected cases. Pending necropsy, whole carcasses should be double-bagged and frozen.

At necropsy, the skin may contain papules, umbilicated pustules (“pocks”) with central necrosis, or crusts over healing lesions. The skin lesions may vary from barely detectable, single small papules to extensive lesions. In some animals, visceral lesions may be seen, including multifocal necrotizing pneumonitis, orchitis, and peripheral lymphadenopathy.

Necropsy lesions have also been described in cynomolgus monkeys given a fatal aerosol dose of monkeypox. In addition to the typical skin lesions, bronchopneumonia was common. The lungs were heavy, congested, and failed to collapse and a dark red, lobular, mottled pattern of edema, atelectasis, and necrosis was seen throughout all of the lobes. In some cases, fibrinous pleuritis or a clear pericardial effusion was also present. Lymph node congestion, peripheral lymphadenopathy, facial exanthema, ulcerative cheilitis, gingivitis, papulovesicular pharyngitis, or ulcerative stomatitis occurred in some animals. The oral lesions, which were most common on the hard palate and the dorsal surface of the tongue, were described as variably sized, depressed, reddened foci of necrosis, erosion, or ulceration surrounded by pale tan to white, slightly raised margins. Some animals had gastritis or 2–3 mm raised lesions with umbilicated necrotic centers on the mucosa of the distal colon or rectum.

Internet Resources

American Veterinary Medical

Association Monkeypox Alert

<http://www.avma.org/pubhlth/monkeypox/default.asp>

Armed Forces Institute of Pathology – Monkeypox

<http://www.afip.org/Departments/infectious/mp/index.html>

Centers for Disease Control and Prevention (CDC) –Monkeypox Index

<http://www.cdc.gov/ncidod/monkeypox/index.htm>

Medical Microbiology

<http://www.gsbs.utmb.edu/microbook>

Monkeypox pages

Center for Infectious Disease Research & Policy (CIDRAP). University of Minnesota

<http://www.cidrap.umn.edu/cidrap/content/hot/monkeypox/index.html>

Pathology of Nonhuman Primates from Primate Info Net. Wisconsin Primate Research Center

<http://www.primate.wisc.edu/pin/pola6-99.html>

Primate Info Net. Wisconsin Primate Research Center

<http://www.primate.wisc.edu/pin/>

References

- “Basic Information about monkeypox.” *Centers for Disease Control and Prevention (CDC)*, June 2003. 27 June 2003 <<http://www.cdc.gov/ncidod/monkeypox/factsheet.htm>>.
- Baskin, G.B. “Pathology of nonhuman primates.” *Primate Info Net*. Feb 2002 Wisconsin Primate Research Center. 27 June 2003 <<http://www.primate.wisc.edu/pin/pola6-99.html>>.
- Baxby, D. “Poxviruses.” In *Medical Microbiology*. 4th ed. Edited by Samuel Baron. New York; Churchill Livingstone, 1996. 27 June 2003 <<http://www.gsbs.utmb.edu/microbook/ch069.htm>>.
- “Case I – 952287 (AFIP 2554549).” *AFIP Wednesday Slide Conference – No. 14. Armed Forces Institute of Pathology*, January 1997. 30 June 2003 <<http://www.afip.org/vetpath/WSC/WSC96/96wsc14.htm>>.
- Cohen, J. “Is an old virus up to new tricks?” *Science* 277, no. 5324 (July 1997): 312–313.
- “Considerations for selection and prioritization of animal specimens for laboratory testing.” *Centers for Disease Control and Prevention (CDC)*, June 2003. 30 June 2003 <<http://www.cdc.gov/ncidod/monkeypox/lab-submissionguid.htm>>.
- Gough A.W., N.J. Barsoum, S.I. Gracon, L. Mitchell and J.M. Sturgess. “Poxvirus infection in a colony of common marmosets (*Callithrix jacchus*). [Abstract]” *Lab. Anim. Sci.* 32, no. 1 (Feb 1982): 87–90.
- “Interim case definition for animal cases of monkeypox.” *Centers for Disease Control and Prevention (CDC)*, June 2003. 30 June 2003 <<http://www.cdc.gov/ncidod/monkeypox/animalcasedefinition.htm>>.
- “Interim guidance for necropsy and animal specimen collection for laboratory testing.” *Centers for Disease Control and Prevention (CDC)*, June 2003. 30 June 2003 <<http://www.cdc.gov/ncidod/monkeypox/necropsy.htm>>.

- Khodakevich L., M. Szczeniowski, J.Z. Manbu–ma–Disu, S. Marennikova, J. Nakano and D. Messinger. “The role of squirrels in sustaining monkeypox virus transmission.” *Trop. Geogr. Med.* 39, no. 2 (April 1987): 115–22.
- “Monkeypox.” *Department of Infectious and Parasitic Diseases. Armed Forces Institute of Pathology*, July 2003. 1 July 2003 <<http://www.afip.org/Departments/infectious/mp/index.html>>.
- “Monkeypox.” *Laboratory Primate Newsletter, Brown University* 36, no. 3 (July 1997). 30 June 2003 <<http://www.brown.edu/Research/Primate/lpn36-3.html#pox>>.
- “Monkeypox backgrounder.” *American Veterinary Medical Association*, June, 2003. 30 June 2003 <<http://www.avma.org/pubhlth/monkeypox/default.asp>>.
- “Monkeypox infections in animals: updated interim guidance for persons who have frequent contact with animals, including pet owners, pet shop employees, animal handlers, and animal control officers.” *Centers for Disease Control and Prevention (CDC)*, June 2003. 30 June 2003 <<http://www.cdc.gov/ncidod/monkeypox/animalhandlers.htm>>.
- “Monkeypox infections in animals: updated interim guidance for veterinarians.” *Centers for Disease Control and Prevention (CDC)*, June 2003. 30 June 2003 <<http://www.cdc.gov/ncidod/monkeypox/animalguidance.htm>>.
- “Multistate outbreak of monkeypox — Illinois, Indiana, and Wisconsin, 2003.” *Morb. Mortal. Wkly. Rep.* 52, no. 23 (June 13, 2003): 537–540. 30 July 2003 <<http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5223a1.htm>>.
- Rand, M.S. “Zoonotic diseases.” *Institutional Animal Care and Use Committee*, University of California, Santa Barbara. 30 June 2003 <<http://www.research.ucsb.edu/connect/pro/disease.html>>.
- Schoeb, T.R. “Diseases of laboratory primates.” 27 June 2003 <<http://netvet.wustl.edu/species/primates/primatel.txt>>.
- “Update: Multistate outbreak of monkeypox — Illinois, Indiana, Kansas, Missouri, Ohio, and Wisconsin, 2003.” *Morb. Mortal. Wkly. Rep.* 52, no. 24 (June 20, 2003): 561–564. 30 June 2003 <<http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5224a1.htm>>.
- “Update: Multistate outbreak of monkeypox — Illinois, Indiana, Kansas, Missouri, Ohio, and Wisconsin, 2003.” *Morb. Mortal. Wkly. Rep.* 52, no. 25 (June 27, 2003): 589–590. 30 June 2003 <<http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5225a4.htm>>.
- “Updated interim CDC guidance for use of smallpox vaccine, cidofovir, and vaccinia immune globulin (VIG) for prevention and treatment in the setting of an outbreak of monkeypox infections.” *Centers for Disease Control and Prevention (CDC)*, June 2003. 30 June 2003 <<http://www.cdc.gov/ncidod/monkeypox/treatmentguidelines.htm>>.
- Zaucha G.M., P.B. Jahrling, T.W. Geisbert, J.R. Swearngen and L. Hensley. “The pathology of experimental aerosolized monkeypox virus infection in cynomolgus monkeys (*Macaca fascicularis*).” *Lab. Invest.* 81 (2001): 1581–1600. 30 June 2003 <<http://labinvest.uscapjournals.org/cgi/content/full/81/12/1581>>.