

Monkeypox

Last Updated: July 2009



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Importance

Monkeypox is a zoonotic viral disease that can infect nonhuman primates, rodents and some other mammals. This disease is endemic in western and central Africa, where it circulates in unknown animal hosts and emerges periodically as a zoonosis in humans. Outbreaks have also been seen occasionally among captive nonhuman primates in other parts of the world. The only outbreak of human monkeypox to be reported outside Africa occurred in the United States in 2003. The virus entered North America in exotic African rodents imported as pets, and spread to pet prairie dogs, which were highly susceptible to infection. The monkeypox virus subsequently infected approximately 70 people who had been in contact with these animals. No outbreaks have been reported in the U.S. since that time, and there is no evidence that the virus has become endemic in North America. Prompt diagnosis of monkeypox is essential, to prevent this disease from becoming established outside Africa, and because it resembles smallpox, a potential bioterrorist weapon.

Etiology

Monkeypox results from infection by the monkeypox virus, a member of the genus *Orthopoxvirus* in the family Poxviridae (subfamily Chordopoxvirinae). Two clades of monkeypox viruses, the West African and Congo Basin viruses, have been identified. The Congo Basin viruses are more virulent. Monkeypox virus is closely related to some other orthopoxviruses such as variola (smallpox) virus, and it cannot be distinguished from these viruses in some laboratory tests.

Monkeypox should not be confused with benign epidermal monkeypox (BEMP), a poxviral disease of primates caused by tanapox virus, an antigenically unrelated virus in the genus *Yatapoxvirus* of the family Poxviridae.

Geographic Distribution

Monkeypox is endemic in central Africa (the Congo Basin) and West Africa. An outbreak of human monkeypox occurred in the U.S. in 2003. In the U.S., cases were seen in pet prairie dogs, other small mammals in captivity, and people who had been exposed to infected prairie dogs. There have been no reports of infections among humans or domesticated animals in North America since 2003, and limited surveys suggest that the virus probably did not enter wild animal populations.

Transmission

The routes of transmission among animals are incompletely understood, but the virus might be transmitted in aerosols, through skin abrasions, or by the ingestion of infected tissues. In prairie dogs, monkeypox virus or its nucleic acids have been found in skin lesions, urine, feces, and oral, nasal and conjunctival exudates. Viral antigens and mature virus particles occur in the lungs and oral lesions of these animals, suggesting that respiratory droplets as well as saliva could be infectious. In dormice, monkeypox virus has been detected in most tissues. Limited evidence suggests that some small animals such as dormice and Gambian giant pouched rats might carry monkeypox virus for a few weeks or months. This virus can be spread on fomites.

Most cases of monkeypox in humans are zoonotic. The monkeypox virus is thought to be transmitted to people in bites from animals, in aerosols during close contact, or by direct contact with lesions, blood or body fluids. In Africa, human outbreaks have often been linked to handling, preparing and eating wild animals. In the U.S., most cases occurred among people who had close direct contact with prairie dogs; some infections were apparently acquired in scratches and bites, or through open wounds. Human-to-human transmission can also occur. Potential routes of transmission between people include skin-to-skin contact, contact with infectious body fluids, or aerosol transmission during prolonged face-to-face contact. Transmission between people appears to be relatively inefficient, and sustained human-to-human spread has not been reported; until 2005, the longest documented chain was four serial transmissions. More efficient person-to-person spread with six serial transmissions was recently reported from an outbreak in the Republic of Congo.

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

The incubation period is 7 to 17 days, with a mean of 12 days, in Africa. In the U.S. outbreak, the incubation period was 4 to 24 days, with a mean of 14.5 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 malaise, fever, chills, headache, sore throat, myalgia, backache, fatigue, lymphadenopathy (most often affecting the submandibular, postauricular, cervical and/or inguinal lymph nodes) and a nonproductive cough. Nausea, vomiting and conjunctivitis were also reported from some cases in the U.S. A rash, initially characterized by macules and papules, develops one to several days after the prodromal signs; these lesions develop into vesicles and pustules (“pocks”), which umbilicate, form scabs and are eventually shed. The number of skin lesions varies from less than 25 to more than a hundred. They are usually concentrated on the extremities (a centrifugal pattern) but can also be seen on the head and torso. Lesions may develop on the mucous membranes, as well as on the palms, soles and genitalia. Confluent rashes and recurrent febrile periods can occur in severe cases. Corneal ulceration, coagulation disorders, respiratory complications including dyspnea, encephalitis (rarely) and multiorgan failure have also been reported. Although most patients survive, some cases end in death. In patients who recover, the illness generally lasts for 2 to 4 weeks, and the skin lesions usually resolve within 14 to 21 days. Residual varioliform scarring, with hypopigmented and/or hyperpigmented skin lesions may be a sequela. Severe scarring, as seen in smallpox, is rare. Subclinical and very mild cases have also been reported.

The 2003 monkeypox outbreak in the U.S., which was caused by a West African strain of the virus, differed in some respects from the classical description of the disease in Africa. Most people in the U.S. had a relatively mild form of the disease, with less marked lymphadenopathy than reported in Africa, relatively few lesions and a self-limiting course. In many patients, the skin lesions were localized and confined to the extremities; generalized rash was rare. Some pustules had

prominent erythematous flares; such flares have not been noted in African cases, possibly because most affected people have darker skin. In the U.S., skin lesions sometimes occurred at a bite or scratch, the apparent inoculation site, before systemic signs developed. The skin lesions usually healed without dyspigmented scars in this outbreak. Two severe cases were reported, both in children. One child developed encephalitis, a complication that had been reported only once before. The other child had generalized lesions including lesions in the oropharynx, and severe cervical and tonsillar lymphadenopathy, which caused difficulty in breathing and swallowing. An adult developed complications of keratitis and corneal ulceration, and received a corneal transplant. Patients with other symptoms of monkeypox and immunological evidence of exposure, but no skin lesions, were described in this outbreak. Unusually, all patients recovered.

Communicability

Little or no person-to-person spread has been seen in some outbreaks, but up to six serial transmissions were reported during a recent outbreak in the Republic of Congo. In people, monkeypox virus has been isolated up to 18 days after the onset of the rash. Infected individuals are assumed to be contagious from 1 day before the rash appears and for up to 21 days after the initial symptoms, or until all scabs have separated and throat swabs are negative by PCR.

Diagnostic Tests

Monkeypox can be tentatively diagnosed if the characteristic skin lesions are present and there is a history of exposure. Electron microscopy identifying orthopoxviruses in skin lesions and immunohistochemistry for orthopoxvirus antigens are suggestive, but the specific virus cannot be identified with these techniques. A definitive diagnosis can be made by isolating the monkeypox virus from skin lesions (e.g., in scabs or material from vesicles) or throat and nasopharyngeal swabs. This virus can be recovered in mammalian cell cultures, and may be identified using polymerase chain reaction (PCR) assays followed by restriction fragment-length polymorphism (RFLP) analysis or sequencing. Monkeypox-specific PCR assays are available in some laboratories, and a DNA oligonucleotide microarray can identify this virus rapidly and specifically. PCR can also be performed directly on clinical samples.

Serology may also be helpful. Convalescent-phase serum can be tested for orthopoxvirus-specific IgM with an enzyme-linked immunosorbent assay (ELISA) if the lesions have resolved. Cross-reactions between orthopoxviruses, including smallpox and monkeypox viruses, can occur in serological tests. Cross-adsorbed virus neutralization, immunofluorescence or hemagglutination inhibition assays, as well as

immunoblotting (Western blotting), can be used to distinguish reactions between monkeypox virus and smallpox virus. A specific ELISA that can diagnose monkeypox in people vaccinated for smallpox has been reported in the literature.

Treatment

Treatment of monkeypox is mainly supportive. The antiretroviral drug cidofovir has been promising *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 (which was used to treat smallpox) in cases of monkeypox is unknown.

Prevention

As a routine preventative measure, care should be taken to treat and cover breaks in the skin when working with nonhuman primates or other animals that may be hosts. Smallpox vaccination, particularly when recent, appears to provide some protection from monkeypox. Post-exposure vaccination also seems to be helpful. The CDC currently recommends this vaccine only for people who have been or are likely to be exposed to monkeypox. The general population is not routinely vaccinated in endemic areas of Africa, as the benefits do not appear to outweigh the risks and expense. Some people, including those with severe T cell immunodeficiencies, may not be able to receive the smallpox vaccine.

Isolation of infected patients, good infection control measures and ring vaccination are helpful in preventing person-to-person transmission. Because the full host range of monkeypox virus is uncertain, it is advisable for infected individuals to limit contact with any pet, particularly species known to be susceptible.

Infection control procedures such as good hygiene, frequent hand washing, and disinfection of surfaces and equipment are important during contact with animals suspected to have this disease. As few people as possible should be exposed. Veterinarians and staff should use personal protective equipment (PPE) including gloves and a gown when examining or treating these animals. Eye protection such as tightly fitted goggles or a face shield is advisable if body fluids might be sprayed. Aerosol transmission can be prevented with a N95 filtering or comparable disposable respirator. If no respirator is available in the clinic, a surgical mask gives some protection from transmission by contact or via large droplets. Veterinarians who do not wish to examine or treat any animal with monkeypox may refer clients to the local or state health department for guidance. Anyone who has been in contact with a monkeypox suspect should contact a health care provider immediately. The local or state health department must also be informed.

Necropsies should be done in Biosafety Level 2 laboratories, using a certified Class II Biological Safety

Cabinet. The person performing the necropsy should have a recent smallpox vaccination and wear PPE. The CDC recommends that veterinarians in private practice avoid performing necropsies or biopsies due to the zoonotic risk. PPE should be used when collecting other types of clinical samples.

Morbidity and Mortality

Monkeypox is thought to be a rare disease in humans; however, unpublished surveillance data suggest that cases may occur more frequently in Africa than the literature indicates. Between 1998 and 2002, 215 possible monkeypox cases were reported to the Democratic Republic of Congo (DRC) Ministry of Health, and 88 were subsequently confirmed by laboratory testing to be this disease. In Africa, monkeypox usually occurs in rural populations, particularly in children. Generally, these infections are seen after contact with wild small mammals, which are caught for food and other purposes.

Most outbreaks 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%. In 1996-1997, an outbreak in the DRC continued for more than a year, with a person-to-person transmission rate estimated at 78%. However, epidemiological evidence suggests that many of the cases in this outbreak may have been chickenpox (varicella); the number of monkeypox cases and the transmission rate might have been overestimated due to self-reporting and the unavailability of laboratory testing. Person-to-person transmission with six serial transmissions was reported during an outbreak of monkeypox in the Republic of Congo (RCG) in 2003; before this time, the maximum number of serial transmissions was four. Sustained transmission of monkeypox virus in human populations has not been reported.

Congo Basin (Central African) strains are reported to cause more severe disease, with higher morbidity, mortality and person-to-person transmission rates, than West African strains. Overall, case fatality rates from 1% to 33% have been reported in Africa. In the DRC (Central Africa), surveillance suggests that the case fatality rate is approximately 10-17%. The highest risk of death is in young children. Monkeypox seems to be less severe in people who have been vaccinated for smallpox, although the protection might decrease with time.

The U.S. outbreak was caused by a West African strain of monkeypox virus. In this outbreak, people became infected after direct contact with pet prairie dogs. One case was originally thought to have been acquired from a rabbit, but testing (unpublished) by the CDC determined that the rabbit was not infected. African rodents were not implicated in direct transmission to humans in this outbreak, although some of these animals had high viral titers. The types of behavioral interactions

with humans may have contributed to this phenomenon. Seventy-two human infections were reported in this outbreak, with 37 of these laboratory confirmed. Most clinical cases were relatively mild. Severe disease occurred in two children, as the result of encephalitis or generalized monkeypox, but no deaths were reported. The availability of advanced health care facilities and good supportive care, as well as the absence of poor nutrition and concurrent diseases, may have contributed to the survival rate. The route of inoculation might also contribute to differences in clinical signs or severity; some people in Africa may be infected by ingestion during food preparation.

Infections in Animals

Species Affected

The monkeypox virus's full host range is unknown. Species known to be susceptible include Old and New World monkeys and apes, a variety of rodents and other small mammals. Among captive primates, infections have been reported in rhesus macaques (*Macaca mulatta*), cynomolgus monkeys (*Macaca fascicularis*), langurs, baboons (*Papio* spp.), chimpanzees (*Pan* spp.), orangutans (*Pongo* spp.), marmosets, gorillas (*Gorilla* spp.), gibbons (family Hylobatidae), owl-faced monkeys (*Cercopithecus hamlyn*), squirrel monkeys (*Saimiri* spp.) and others.

In 2003, a West African strain of monkeypox virus was introduced into the U.S. in a shipment of imported exotic mammals from Africa. Infected animals in this shipment included Gambian giant pouched rats (*Cricetomys* spp.), rope squirrels (*Funisciurus* sp.) and dormice (*Graphiurus* sp.). Whether a species originally harbored the virus or became infected during shipment is unknown. Two cusimanse (*Crossarchus obscurus*), a genet (*Genetta genetta*) and 27 sun squirrels (*Heliosciurus gambianus*) from this shipment had no evidence of infection. North American black-tailed prairie dogs (*Cynomys ludovicianus*) were readily infected by this virus. Infections were also documented in a groundhog/ woodchuck (*Marmota monax*), an African hedgehog (*Atelerix* sp.), a jerboa (*Jaculus* sp.), and two opossums (*Didelphis marsupialis*, a species native to South America, and the gray short-tailed opossum, *Monodelphis domestica*). Species that developed antibodies after exposure, but had no evidence of viral DNA or infectious virus, included chinchillas (*Chinchilla lanigera*) and coatimundis (*Nasua nasua*). Many other species were exposed but did not become seropositive. Experimental infections have been established in prairie dogs, dormice, ground squirrels (*Spermophilus tridecemlineatus*), the cotton rat (*Sigmodon hispidus*) and the multimammate mouse (*Mastomys natalensis*).

The natural reservoir hosts for the monkeypox virus remain to be determined. Two genera of African squirrels,

Funisciurus spp. (rope squirrels) and *Heliosciurus* spp. (sun squirrels), have high seroprevalence rates, and have been suggested as possible maintenance hosts or vectors. Rope squirrels were also among the infected species during the outbreak in the U.S. Sun squirrels in the same shipment had no evidence of infection; however, it is possible that they are reservoir hosts only for the Congo Basin clade and not the West African clade. In Africa, antibodies to monkeypox virus have also been found in other rodents and shrews, as well as nonhuman primates. Whether these animals maintain the infection in the wild, or are incidental hosts, is unknown.

Incubation Period

The incubation period is 4 to 12 days in experimentally infected black-tailed prairie dogs and 4 to 5 days in experimentally infected ground squirrels. In one study, experimentally infected cynomolgus monkeys developed clinical signs 6 to 7 days after aerosol exposure to a lethal dose of virus.

Clinical Signs

Nonhuman primates

In nonhuman primates, monkeypox usually occurs as a self-limiting rash. The initial clinical signs are a fever and 1-4 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. Some animals have only skin lesions. In more severe cases, coughing, nasal discharge, dyspnea, anorexia, decreased body weight, facial edema, oral ulcers or lymphadenopathy may also be seen. Disseminated disease with visceral lesions is uncommon in natural infections among nonhuman primates. Pneumonia is common only in monkeys infected experimentally via aerosols.

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

Prairie dogs

In prairie dogs, the clinical signs may include fever, depression, anorexia, weight loss, nasal discharge, sneezing and/or coughing, respiratory distress, a nodular skin rash and oral ulcers. During the outbreak in the U.S., blepharoconjunctivitis was often the first sign. In experimentally infected prairie dogs, skin lesions appeared first on the head or extremities, followed by the trunk (a centrifugal pattern), similarly to humans. On the trunk and limbs, characteristic monkeypox lesions developed from macules through vesicles and pustules

before forming scabs. Macules and vesicles also occurred on the face in this experiment, but pustules were not seen. Lymphadenopathy has been reported in naturally infected prairie dogs, but this sign was absent in some animals after experimental inoculation. Some experimentally infected prairie dogs died 1 to 2 weeks after infection without developing lesions on the skin or mucous membranes. Some naturally or experimentally infected animals have recovered.

Other rodents

In dormice inoculated intranasally, the clinical signs were limited to lethargy, an unkempt hair coat, a hunched posture, conjunctivitis and dehydration; many infections were fatal. Experimentally infected cotton rats developed acute clinical signs including rhinitis, conjunctivitis, dyspnea, coughing and progressive emaciation, often ending in death. In ground squirrels, the first clinical signs were anorexia and lethargy. Nasal hemorrhages and dyspnea were common in ground squirrels inoculated with the Congo Basin isolate, but nasal hemorrhages were uncommon with the West African strain, and respiratory distress occurred only terminally. Both strains were uniformly fatal at the dose used. Fatal infections were also reported among rope squirrels and one Gambian giant pouched rat in the shipment of exotic African rodents to the U.S. Mild symptoms, with no respiratory signs and limited skin lesions, were seen in another Gambian giant pouched rat in the shipment. Other pouched rats that appeared healthy were also seropositive.

Communicability

Infected animals are assumed to be contagious 1 day before and up to 21 days after the initial signs, or until all skin lesions have formed scabs and no other clinical signs are present. In experimentally infected prairie dogs, West African or Congo Basin monkeypox virus can be shed until 21 days after inoculation. Limited evidence suggests that some dormice and other animals might carry monkeypox virus for weeks or months. One dormouse had evidence of viral DNA in tissues, urine and feces by PCR for at least 6 months, but no viral antigens were found when this animal was euthanized. Whether such animals shed infectious virus is unknown.

The CDC recommends that animals that have been exposed to monkeypox be quarantined for six weeks after exposure.

Diagnostic Tests

In the U.S., diagnostic samples for monkeypox are submitted through the state health department, which should be contacted before collecting or shipping any samples. Tissues and other specimens must be packaged and shipped under secure conditions to prevent infections in humans and animals. Shipment must comply with all local, state and federal regulations.

Monkeypox can be tentatively diagnosed if the characteristic skin lesions are present, or if other clinical signs consistent with the disease are seen during an outbreak. Histopathology provides supportive evidence. The diagnosis can be confirmed by virus isolation or PCR. Monkeypox virus can be recovered in mammalian cell cultures, and may be identified using PCR followed by RFLP analysis or sequencing. Monkeypox-specific PCR assays are available in some laboratories. PCR can also be performed directly on clinical samples. If the animal has not been exposed to other orthopoxviruses, monkeypox can be tentatively diagnosed by detecting orthopoxvirus virions with electron microscopy or orthopoxvirus antigens by immunohistochemistry.

Serum, samples of skin lesions and conjunctival swabs may be collected from live animals. Monkeypox virus has also been detected in blood, and sometimes in oral and nasal secretions (e.g., oropharyngeal swabs), urine and feces. At necropsy, tissues should be collected from all organs that have lesions. One set of tissues should be collected into 10% formalin for histopathology. A second set should be collected aseptically for virus isolation. Transport medium should not be used with the latter set of tissues. In prairie dogs, monkeypox viruses, viral DNA or antigens have been detected in blood, skin lesions, eyelid and tongue samples, and many internal organs including the lung, liver, spleen and lymph nodes. In dormice, monkeypox viruses have been found in most organs and tissues. One study suggested that the liver contained particularly large amounts of virus in this species. In experimentally infected ground squirrels, monkeypox antigens could be detected by immunohistochemistry in the lung, liver, lymphoid organs, esophagus and intestines. Samples for virus isolation should be refrigerated, or they may be frozen if they will not be shipped for more than 24 hours.

Treatment

During the 2003 outbreak, the CDC recommended that all animals with suspected monkeypox be euthanized to prevent zoonotic infections and to reduce disease transmission to other animals. Nonhuman primates are not necessarily euthanized during outbreaks in facilities. Treatment is supportive. Some animals recover spontaneously.

Prevention

Six types of African rodents – sun squirrels (*Heliosciurus* sp.), rope squirrels (*Funisciurus* sp.), dormice, Gambian giant pouched rats, brush-tailed porcupines (*Atherurus* sp.), and striped mice (*Hybomys* sp.) can no longer be imported into the U.S. except for scientific purposes, education or exhibition under a permit from the CDC. This ban applies to these animals whether they were born in Africa or on another continent. These animals, as well as prairie dogs, can no longer be transported, sold, distributed or released into the

environment on either public or private property. Embargoed animals can be taken to a veterinarian, government official or animal control office under permission from the health department.

Good infection control measures, including the isolation of new animals, help prevent outbreaks in primate facilities. Care should be taken to avoid spreading the virus on fomites. Vaccination with vaccinia virus is protective. Because infections have been reported in Asian monkeys when they were mixed with primates from Africa, these species should not be housed in the same area. Anyone who has been exposed to monkeypox should avoid contact with animals, particularly rodents and nonhuman primates, to avoid transmitting the disease to them.

During an outbreak, monkeypox may be controlled by quarantines of infected animals and tracing of their contacts. Areas where these animals have been kept should be cleaned and disinfected; specific instructions are available from the state or local health department, or the CDC Web site. Animals that have been in contact with a monkeypox-infected animal may be placed under quarantine for 6 weeks from the date of the last exposure.

During outbreaks, veterinarians should remain aware of current recommendations from their state and local health departments. During the 2003 outbreak in the U.S., some states recommended that animals with suspected monkeypox not be taken to veterinary hospitals, to prevent human exposure. Animals that may have this disease should never be brought to a veterinary clinic without first contacting the clinic so that precautions may be taken. To avoid exposing other people and animals, the animal should enter the facility through a separate area. When it is transported, it should be kept in a cage (or box with air holes) and handled using heavy rubber gloves and a long-sleeved shirt to prevent scratches and exposure to body fluids. If the animal is likely to bite, heavier gloves would be appropriate. In the clinic, monkeypox suspects should be kept isolated, and handled using PPE. If the animal has died, the carcass should be double-bagged and frozen pending necropsy. For additional preventative measures, see “Infections in Humans.”

Morbidity and Mortality

The prevalence of infection in wild primates is unknown. In one study, 8% of nonhuman primates in Africa were seropositive. Few outbreaks have been reported among captive primates. The morbidity rate is usually high and the mortality rate low; most adult animals recover. More severe illness may be seen in infants, which may die, as well as in cynomolgus monkeys, orangutans, and primates of all ages infected experimentally via aerosols. Cynomolgus monkeys developed more severe clinical signs after inoculation with a Congo Basin than a West African strain.

Prairie dogs appear to be very susceptible to monkeypox. In black-tailed prairie dogs, the mortality rate was 50% in animals inoculated subcutaneously with a Congo Basin strain, and 25% in animals inoculated intranasally. Prairie dogs infected with a West African strain by either route did not die in this experiment. In another study, intranasal inoculation of a West African strain resulted in 60% mortality in prairie dogs, and intraperitoneal inoculation was uniformly fatal. In the U.S. outbreak, which was caused by a West African strain, some prairie dogs died rapidly, but others recovered.

In Africa, monkeypox infections may be particularly common among squirrels; antibodies have been found in 24-50% of rope squirrels (*Funisciurus* spp.) and 15-50% of *Heliosciurus* spp squirrels. Fatal infections have been reported in rope squirrels, but the mortality rate in this species is unknown. Infections have also been documented among Gambian giant pouched rats and dormice. In one study, 16% of giant pouched rats in Africa were seropositive. During the outbreak in the U.S., monkeypox virus was found in one giant pouched rat that died soon after arrival. Another member of this species had a very mild illness, and orthopoxvirus antibodies were found in 12 of 18 healthy animals after the outbreak. In dormice inoculated intranasally with 2-200 PFU of virus per animal, the mortality rate was dose-dependent and varied from 38% to 100%. A lower dose (0.2 PFU/dormouse) did not result in any deaths.

Experimental infections have been reported in other species of rodents. Cotton rats inoculated by the intranasal route developed acute disease with a mortality rate of 50% after intranasal inoculation and 100% after intravenous inoculation. Ground squirrels had more severe clinical signs after inoculation with a Congo Basin strain than a West African strain, but both strains resulted in 100% mortality.

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

Due to the risk of infection, the CDC recommends that practicing veterinarians avoid performing necropsies or biopsies on suspected cases. Pending necropsy, whole carcasses should be double-bagged and frozen. Animals should be necropsied only by individuals who have a current smallpox vaccination, and the biological safety guidelines recommended by the CDC (<http://www.cdc.gov/ncidod/monkeypox/necropsy.htm>) should be followed.

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 including multifocal necrotizing pneumonitis, orchitis and peripheral lymphadenopathy may be seen.

In cynomolgus monkeys given a fatal aerosol dose of monkeypox, necropsy lesions commonly included both skin lesions and bronchopneumonia. 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 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 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.

Blepharoconjunctivitis is a common finding in prairie dogs. As well as skin lesions, ulcers may be found on the tongue and hard palate. Bronchoalveolar pneumonia with patchy red-brown consolidation, and enlargement of the cervical and thoracic lymph nodes, have been reported in some animals. The visceral pleura may contain 1–3 mm white plaques, and small (2–3 mm) white, firm, deeply embedded foci with umbilicated necrotic centers have been reported in the intestines and glandular portion of the stomach.

In intranasally inoculated dormice, the gross lesions at necropsy included hepatomegaly, lymphadenopathy and hemorrhages in the upper gastrointestinal tract, nasal cavity, gall bladder and brain. Pulmonary edema and hemorrhages were reported in experimentally infected ground squirrels. In multimammate mice, hemorrhagic pleuritis or peritonitis and inflammatory hyperemia were described in many organs after intraperitoneal inoculation.

Internet Resources

- Center for Infectious Disease Research & Policy (CIDRAP).
University of Minnesota. Monkeypox
<http://www.cidrap.umn.edu/cidrap/content/hot/monkeypox/index.html>
- Centers for Disease Control and Prevention (CDC).
Monkeypox
<http://www.cdc.gov/ncidod/monkeypox/index.htm>
- Medical Microbiology
<http://www.gsbs.utmb.edu/microbook>
- Wisconsin National Primate Research Center
<http://www.primate.wisc.edu/>

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