

ORIGINAL RESEARCH**To study the monkey pox virus: A review study**

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Abstract

The monkey pox virus is an orthopox virus that may be transmitted to humans and causes symptoms similar to those of smallpox but with a far lower mortality rate. Native to western and central Africa, this virus has caused epidemics in the Western Hemisphere due to exposure via the trade of exotic pets and international travel. Poxviruses have the form of cubes and are encased in a lipoprotein shell that protects a DNA genome that runs in a straight line. Poxvirus genomes encode all proteins necessary for replication, transcription, assembly, and egress; they just depend on host ribosomes for mRNA translation. Similar to smallpox, monkey pox causes a fever, headache, myalgia, tiredness, and lymphadenopathy. After 1–2 days, mucosal lesions appear in the mouth, followed by concentrically located lesions over the face and extremities (especially the palms and soles). The number of lesions, which may range from a few hundred to several thousand, might vary widely depending on whether or not the rash spreads all over the body. It is recommended that the infected individual remain in isolation, wear a surgical mask, and keep lesions covered as much as possible until all crusts on lesions spontaneously break off and a new skin layer emerges. Drugs shown to be effective in animal studies against orthopox viruses and severe vaccinia vaccine after effects may be considered for experimental use in very rare cases. Whether or if the monkey pox virus can be eradicated by the intravenous administration of vaccinia immune globulin, brincidofovir, or tecovirimat, an oral inhibitor of intracellular viral release, remains unknown.

Keywords: Monkey pox, zoonotic, lymphadenopathy, Rash, PCR

Introduction

The viral infection known as monkey pox may be transmitted to humans and results in a rash very similar to that of smallpox. The risk of spreading monkey pox to those outside of an infected family and of dying as a result of an illness is, however, far lower than it is with smallpox. In addition to secondary syphilis, herpes simplex infection, and varicella-zoster virus infection, a monkey pox rash may mimic other common infectious rashes. The monkey pox virus is a kind of orthopox virus, which also includes variola and vaccinia viruses in its family tree.¹

Evidence from humans, animals, and molecular biology point to the existence of two distinct monkey pox strains in Africa.¹ Diseases caused by Clade I have been connected to the Congo basin, whereas Clade II has only been seen in West Africa. There are several genes absent from the West African strain that are present in the Central African strain, making it less dangerous.² Another clade 2 related strain may have been found in the 2022 pandemic that swept over Europe and North America. Three preliminary studies of viruses from this pandemic have shown sequence similarities to strains that were widespread in Nigeria in 2018-2019.³

Epidemiology

The first case of monkey pox was discovered in the late 1950s in Denmark, where it had been obtained from a group of Singaporean lab monkeys that had been imported for polio virus study.⁴ In the 1970s, the Democratic Republic of the Congo was the first place in which monkey pox was identified as a human health risk. After the smallpox vaccination was no longer available, Central and West Africa became the epicentre of the disease's spread.⁵ The United States saw the first ever monkey pox pandemic in the Western hemisphere in 2003. After over 40 years with no reported cases, monkey pox has returned to Nigeria in 2017.⁶ Travellers returning from places where the disease is not prevalent have reported contracting this pandemic. There have been a few rare instances of monkey pox reported by travellers returning from endemic areas. There were six cases of monkey pox in the United Kingdom between 2018 and 2021. Four of these were linked to visitors from monkey pox endemic countries, two were the result of household transmission from one of the index cases, and one was a healthcare worker who contracted the disease while on the job.⁷ In July of 2021, a case of monkey pox was confirmed in Dallas, Texas.⁸ A new outbreak of monkey pox was documented in Europe in the month of May 2022. There have been reported cases in non-endemic nations throughout the world, suggesting community-wide spread of the pandemic.⁹ On July 23, 2022, the World Health Organization declared this monkey pox pandemic a global public health emergency. By July of 2022, tens of thousands of confirmed cases of monkey pox/orthopoxvirus had been documented in dozens of nations.¹⁰

Transmission

Animal-to-human transmission

The monkey pox virus spreads most often by a bite or through contact with an infected animal's bodily fluids. Cooking bush meat is another option. Several different types of monkeys, as well as rope squirrels, tree squirrels, Gambian pouched rats, dormice, and other primates, have been shown to be infected with the monkey pox virus throughout Africa.¹¹ Accidental hosts include humans and monkeys; the reservoir is probably rodents. The severity of clinical indications of monkey pox infection seems to be related to the quantity of exposure, as was highlighted by the 2003 prairie dog pandemic in the United States. In one study, for instance, researchers divided prairie dog exposures into two categories: non-invasive (such as when a person touched an infected animal or cleaned its cage) and "complex" (eg, invasive bite or scratch from an ill prairie dog).¹² Systemic disease was more

common in persons with more involved exposures compared to those with less involved exposures.

Human-to-human transmission

Direct contact

Transmission is believed to occur most often via contact with infected open wounds, scabs, or bodily fluids.¹³ Therefore, monkey pox may be transferred when people are in close touch with one another. A possible route of entrance might be via microabrasions in the mucous membranes.

Indirect contact through fomites

Clothing or linens contaminated with infectious material from bodily fluids or wounds are examples of fomites that might facilitate spread.¹³

Respiratory secretions

Monkey pox virus is also thought to be spread through respiratory secretions, although prolonged face-to-face contact may be required for transmission to occur via this route.⁸

Vertical transmission

Although the rate of transmission or danger per trimester is unknown, the virus may pass the placenta from the mother to her foetus, resulting in congenital monkey pox. In the 2022 epidemic, viral DNA was found in semen, confirming that the disease propagated via this route as well as through vaginal secretions.¹⁴

Clinical manifestations

The vast majority of those who had monkey pox during the global pandemic of 2022 displayed classic symptoms. It seems that infections without symptoms are unusual.¹⁵

Incubation period

Depending on the individual, the incubation time for monkey pox virus infection might be anywhere from 5 days to 21 days.

Signs and symptoms

Typical symptoms of monkey pox include a systemic illness characterised by high body temperature, chills, and muscle aches, as well as a rash that may be easily recognised from other vesicular eruptions (eg, herpes simplex, varicella, and smallpox). Some people during the first outbreak of monkey pox illness in May 2022 presented with vaginal, rectal, and/or oral lesions without the traditional prodrome.¹⁶

Prodromal period

Fevers, severe headaches, lymphadenopathy, back pain, myalgia, and extreme weariness are common during the prodromal stage (which may continue up to five days). Lymph node swelling may be widespread (affecting many distinct parts of the body) or more localised (affecting only one or two regions).

Rash

Rash without a prodrome has been described, but often develops after 1-4 days following the onset of fever and lasts 2-3 weeks. Disease has broken out at the point of injection without a preceding prodrome in the 2022 epidemic. From a few hundred to a few thousand lesions have been identified. When lesions join together, they may cause significant areas of skin to

peel away. While the rash is most noticeable on the face, it may also appear on the hands and feet. In addition to the mouth and throat, vaginal and avulsion sites are possible.¹⁷

Lesions progress through several stages

1. The rash usually starts as 2 to 5 mm diameter macules.
2. Then progresses to papules, vesicles, and finally pustules. Lesions are well-defined, deep-seated, and often develop umbilication (a central depression on the top of the lesion).
3. Eventually, the lesions crust over, and the crusts dry up and fall off. This usually happens 7 to 14 days after the rash appears.

On any particular portion of the body, the lesions often start out and progress together at the same time. However, not all lesions were at the same stage of development during the worldwide monkey pox epidemic that started in May 2022. Although the monkey pox rash is often characterised as painful, it may also become irritating during the crusting stage of the healing process.¹⁸

Complications

Monkey pox has been linked to a number of sequelae, including secondary infections, bronchopneumonia, sepsis, encephalitis, and corneal infections that result in vision loss. Viral strain might also affect the clinical disease.¹¹

Diagnosis

The diagnosis of monkey pox takes into account epidemiologic, clinical, and laboratory findings.

Clinical diagnosis

Other rash disorders, such as chickenpox, measles, bacterial skin infections, scabies, syphilis, and medication-related allergies, must be considered in the clinical differential diagnosis. Lymphadenopathy may differentiate monkey pox from chickenpox or smallpox during the prodromal stage of sickness.¹⁹

Polymerase chain reaction (PCR)

The primary laboratory test is polymerase chain reaction (PCR) testing of skin lesion samples. PCR blood tests are frequently inconclusive since the virus only stays in the blood for a brief period of time. Date of commencement of fever, date of beginning of rash, date of specimen collection, current stage of rash, and patient age are all needed to interpret test findings.¹⁹

Serologic testing

Whenever possible, viral testing should be utilised to confirm a diagnosis of monkey pox, although serologic testing may also be used to do so. It is common practise to consult with local health authorities before deciding to undergo serologic testing. Detectable amounts of anti-orthopoxvirus IgM antibody are commonly seen in patients with monkeypox between day 4 and day 56 after the rash first appears. The Centers for Disease Control and Prevention (CDC) developed an IgM capture ELISA and an IgG ELISA to detect recent monkey pox virus infection. IgM and IgG antibodies in the serum were found 5 and 8 days after the rash first appeared.²⁰

Electron microscopy

Orthopoxvirus can also be identified through electron microscopy, in which characteristic brick-shaped poxvirus virions can be seen.

Histopathologic analysis

Histopathologic analysis may demonstrate ballooning degeneration of keratinocytes, prominent spongiosis, dermal edema, and acute inflammation; however, these findings can also be seen in other viral infections.²¹

Differential diagnosis

Several infections need to be considered in the differential diagnosis of monkey pox; these include

Varicella

Due to the global elimination of smallpox, varicella should be considered as the most probable diagnostic consideration in a patient presenting with a vesicular rash (chickenpox). There have been many outbreaks where telling them apart has been challenging.¹⁴ Lymphadenopathy is often a more prominent symptom of monkey pox than varicella, which might be useful in distinguishing between the two illnesses.

Herpes simplex virus (HSV)

Like monkey pox, herpes simplex virus (HSV) may cause sores in the mouth and genitalia. Those suffering from recurrent HSV often have very minor symptoms, in contrast to those suffering from primary HSV who may experience more severe systemic symptoms such as fever and myalgias. Available polymerase chain reaction (PCR) testing of the lesions is the gold standard for confirming a diagnosis of herpes simplex virus infection.

Smallpox

Considering smallpox as a potential diagnosis in a patient presenting with a pox-like rash is crucial in light of bioterrorism fears. One of the most defining characteristics of monkey pox is lymphadenopathy, which has been seen in almost all cases.⁵

Infections with other poxviruses

Tanapox, another African poxvirus, may also produce a febrile prodrome and skin lesions that clear up within a few weeks without leaving scars.

Varicella

Given the worldwide eradication of smallpox, the most likely diagnostic consideration in a patient presenting with a vesicular rash is varicella (chickenpox). In several outbreaks, it has been difficult to distinguish the two.¹⁴ One feature that may help distinguish these infections is lymphadenopathy, which is often a distinctive feature of monkey pox compared with varicella.

Herpes simplex virus

Herpes simplex virus (HSV) can present with both oral and genital lesions, similar to monkey pox. Although persons with primary HSV may present with systemic symptoms such as fever and myalgias, those with recurrent HSV typically have milder symptoms. The best way to confirm the diagnosis of HSV infection is through polymerase chain reaction (PCR) testing of the lesions, which is readily available.

Smallpox

Because of concerns regarding bioterrorism, it is also important to consider the possibility of smallpox in the differential diagnosis of a patient presenting with a pox-like rash.

Lymphadenopathy, which has been observed in the majority of patients with monkeypox, is a key distinguishing feature.⁵

Other pox viruses

Also in the differential diagnosis is tanapox, another African poxvirus that causes a febrile prodrome and skin lesions that resolve over several weeks without sequelae.

Treatments

Antiviral therapy

Currently, tecovirimat is the recommended treatment, however some specialists may recommend a combination of tecovirimat and cidofovir for individuals with advanced illness. Officials in charge of public health should be consulted before deciding on a treatment regime.

Tecovirimat

An essential orthopoxvirus protein, essential for viral proliferation inside an infected host, is inhibited extremely effectively by the drug tecovirimat. In July 2018, the CDC received a licence to distribute tecovirimat in the United States for the treatment of smallpox.^{22,23} The recommended dose of tecovirimat is determined by the patient's weight, as stated on the product label and in the Lexicomp drug information monograph available on UpToDate. The duration of treatment is 14 days.

Cidofovir/brincidofovir

Animal models have shown that cidofovir is effective against a lethal monkeypox challenge, and it has shown effectiveness in vitro. However, it has not been shown to be useful in clinical trials to treat monkeypox in humans, and it may be associated with major adverse effects, such as nephrotoxicity. In June of 2021, the FDA approved brincidofovir for use in the treatment of smallpox. The clinical availability of brincidofovir, an oral cidofovir analogue, is still unclear.²⁴

Orthopox virus vaccines

Types of vaccines

Two vaccines exist to help reduce the likelihood of contracting monkeypox. Vaccines like ACAM2000 and MVA (modified vaccinia Ankara) (JYNNEOS in the United States, IMVANEX in the European Union, and IMVAMUNE in Canada).

MVA vaccine

Made from a highly attenuated, non-replicating vaccinia virus, the MVA vaccination has been shown to be very safe, especially for people who are immune compromised or who suffer from skin problems. The MVA vaccine requires two doses, given four weeks apart, to be fully effective. Smallpox and monkeypox vaccination JYNNEOS has been approved for use in the USA.

ACAM 2000

Replication-competent smallpox vaccine ACAM2000 has been related to more severe side effects than the MVA vaccination and can only be delivered to certain individuals. U.S. regulators have given the green light to use ACAM2000 for smallpox vaccination purposes. A request for the CDC's approval to use it as a treatment for monkey pox must be made via the IND process, which allows for prolonged access to the medicine.

Prevention

Given the similarities between monkey pox and smallpox viruses, it is hypothesised that immunisation against smallpox will also prevent humans from contracting monkey pox. ²⁵ Since widespread vaccination against smallpox was discontinued after the disease was eradicated, there is no conclusive evidence that this is true of the human population. The chance of contracting monkey pox is reduced after immunisation against smallpox, at least among previously immunised Africans. Monkey pox is spreading because populations' resistance to poxviruses is waning. Cross-protective immunity among those who were vaccinated before to 1980, when mass smallpox vaccinations were halted, has been on the decline since then, and this is being blamed on the continually increasing proportion of unvaccinated individuals. ²⁵ Anyone studying monkey pox outbreaks or providing care for infected humans or animals is encouraged by the centers for Disease Control and Prevention (CDC) to be vaccinated against smallpox. Those who have come into direct contact with infected humans or animals, whether via work or play, should also get the vaccine. ²⁶ Pre-exposure vaccination is not recommended by the CDC for veterinarians, veterinary employees, or animal control officers who have not been exposed to the disease. No safe smallpox or monkey pox immunisation exists at this time. ^{26,27} The centers for Disease Control and Prevention (CDC) recommends that all healthcare workers wear full PPE before interacting with an infected patient (PPE). Included are a robe, mask, goggles, and a respirator with a disposable filter (such as an N95). An infected person has to be isolated in a negative air pressure chamber or, at the at least, a private exam room, to prevent the spread of the disease. ²⁸

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