

Mpox (Monkeypox) is a zoonotic orthopoxvirus that incidentally causes disease in humans similar to smallpox, although with notably lower mortality. This virus is clinically relevant because it is endemic to western and central Africa, with outbreaks in the Western Hemisphere related to the exotic pet trade and international travel.

The mpox (monkeypox) virus was first isolated and identified in 1959 when monkeys shipped from Singapore to a Denmark research facility fell ill. However, the first confirmed human case was in 1970 when the virus was isolated from a child in the Democratic Republic of Congo suspected to have smallpox.

You can listen to the BioTalk on Monkeypox above.

Coincident immunity to the mpox virus was previously achieved with vaccinia vaccination; however, eradicating smallpox and subsequent lack of vaccination efforts paved the way for mpox to gain clinical relevance. Furthermore, because most cases of mpox occur in rural Africa, suspected underreporting may translate to an underestimation of the potential threat of this pathogen.

Etiology

Mpox belongs to the family: *Poxviridae*, subfamily: chordopoxvirinae, genus: orthopoxvirus, and species: mpox virus. Mpox is a zoonosis and is spread from animals to humans. The animal reservoir for the disease is thought to include squirrels, rats, monkeys, primates, prairie dogs, hedgehogs, pigs, and mice found in the African regions from where mpox was previously widely reported. The ongoing epidemic is, however, primarily driven by human-to-human transmission through respiratory droplets, fomites, and direct contact with lesions of an infected individual. Recent analysis has found that viral loads are high in bodily fluids, including urine, saliva, semen, and feces, as well as in swabs taken from the oropharynx and rectum, suggesting that sexual transmission is a major driver of transmission.

Epidemiology

Mpox was a zoonotic disease endemic to central and western Africa and most concentrated in the Democratic Republic of Congo. Although first identified in captive monkeys (hence the name), the available data suggests African rodents as the natural reservoir. Infections have occurred in squirrels, rats, mice, monkeys, prairie dogs, and humans. Currently, two genetically distinct clades have been identified. The Congo Basin (Central African) clade is reported more frequently than the West African clade and has documented cases of human-to-human transmission, whereas the West African clade does not.

Sporadic clusters and cases of human mpox have occurred outside of Africa. In 2003, Gambian giant rats imported from Ghana infected co-habitant prairie dogs sold as household pets in the Midwestern United States. This resulted in fifty-three human cases of mpox. In October 2018, one case occurred in a man who traveled from Nigeria to Israel. In May 2019, one case occurred in a man who traveled from Nigeria to Singapore.

In May 2021, a family returned to the United Kingdom after traveling to Nigeria, and three family members became infected with the mpox virus. The sequential timing of symptom development in each case within the family (day 0, day 19, day 33) could represent human-to-human transmission. In July 2021, one case occurred in a man who traveled from Nigeria to Texas. In November 2021, one case occurred in a man who traveled from Nigeria to Maryland. As of May 2022, one case of human mpox in a man who returned to Massachusetts from Canada is under investigation, as well as clusters of human mpox in the United Kingdom.

Precise prevalence and incidence are difficult to establish, given suspected shortcomings in disease reporting and confirmation. However, both metrics have increased since the discontinuation of routine smallpox vaccination. Demonstrated risk factors for mpox infection are living in heavily forested and rural areas of central and western Africa, handling and preparing bushmeat, caregiving to someone infected with the mpox virus, and not being vaccinated against smallpox. Male gender has also been correlated with infection risk. However, this may be confounded by the cultural norm that men frequently hunt and contact

wild animals.

In 2022, there is now an ongoing Mpoxy outbreak involving multiple countries on different continents, predominantly in the men who have sex with men (MSM) population, with a presentation involving predominantly genital lesions. In a cohort of 595 confirmed cases of Mpoxy in Spain in 2022, 99% of cases were found to be in the MSM population, with the lesions predominantly affecting the genital, perineal, or perianal areas. The study also identified inguinal lymphadenopathy as a predominant feature suggesting that sexual transmission was the main mode of transmission. Germany reported 1304 confirmed cases as of 6th July 2022, again mainly in the MSM population. Sequencing data from various countries suggests that the 2022 epidemic is caused by the West African clade of the Mpoxy virus. However, emerging data suggest that the present outbreak may have a newly emerging clade.

Transmission can occur through contact with bodily fluids, skin lesions, or respiratory droplets of infected animals directly or indirectly via contaminated fomites. Although human-to-human transmission has previously been limited, mathematical modeling in the context of decreasing herd immunity to orthopoxviruses reflects an increasing threat of disease spread between humans. The Centers for Disease Control and Prevention (CDC) recommends isolation in a negative pressure room and standard, contact, and droplet precautions in the healthcare setting with escalation to airborne precautions if possible.



Pathophysiology, History and Physical

Following viral entry from any route (oropharynx, nasopharynx, or intradermal), the mpox virus replicates at the inoculation site and then spreads to local lymph nodes. Next, an initial viremia leads to viral spread and the seeding of other organs. This represents the incubation period, typically lasting 7 to 14 days with an upper limit of 21 days.

Symptom onset correlates with a secondary viremia leading to 1 to 2 days of prodromal symptoms such as fever and lymphadenopathy before lesions appear. Infected patients may be contagious at this time. Lesions start in the oropharynx and then appear on the skin.

Serum antibodies are often detectable by the time lesions appear.

Historical clues for mpox infection, such as recent travel to endemic areas, interaction with wild animals imported from endemic areas, and providing care to an infected animal or human, help build a differential diagnosis, but clinical features are critical.

Initial symptoms include fever, headache, myalgia, fatigue, and lymphadenopathy, a key differentiating feature of mpox from smallpox. After 1 to 2 days, mucosal lesions develop in the mouth, closely followed by skin lesions of the face and extremities (including palms and soles), and are centrifugally concentrated. The rash may or may not spread to the rest of the body, and the total number of lesions may vary from a small amount to thousands.

Over the following 2 to 4 weeks, the lesions evolve in 1 to 2-day increments through macular, papular, vesicular, and pustular phases. Lesions change synchronously and are characterized as a firm, deep-seated, and 2 to 10 mm in size. Lesions remain in the pustular phase for 5 to 7 days before crusts begin to form. Crusts form and desquamate over the subsequent 7 to 14 days, and the condition resolves around 3 to 4 weeks after symptom onset in most cases. Patients are no longer considered infectious after all crusts fall off.

Different reports have suggested that the MSM population is at particular risk in the present outbreak. The predominant clinical features include vesicular, umbilicated, and pseudo-pustular lesions on the skin, fever, weakness, tiredness, headache, and regional lymphadenopathy. The genital or perianal area is commonly involved and has lesion clustering, which is thought to be due to the sexual nature of transmission.

Evaluation

The CDC established case definition criteria for human mpox during the 2003 outbreak in the United States. However, the same criteria are not necessarily as valuable in endemic areas. The specificity of the epidemiological criteria decreases as the potential exposure of the population to infected mammals or humans increases. In addition, the specificity of the clinical criteria decreases as the prevalence of similar illnesses increases, as is the case with

chickenpox, given the lack of routine varicella-zoster vaccination in Africa. Although clinical and epidemiologic criteria remain under review and may differ by situation and geographic location, confirmation of human mpox infection requires laboratory evidence.

Treatment / Management

Currently, there are no specific clinically proven treatments for mpox infection. As with most viral illnesses, the treatment is supportive symptom management. There are, however, prevention measures that can help prevent an outbreak. The infected individual should remain in isolation, wear a surgical mask, and keep lesions covered as much as reasonably possible until all lesion crusts have naturally fallen off and a new skin layer has formed. For severe cases, investigational use can be considered for compounds with demonstrated benefit against orthopoxviruses in animal studies and severe vaccinia vaccine complications.

For individuals exposed to the virus, temperature and symptoms should be monitored twice daily for 21 days because that is the accepted upper limit of the mpox incubation period. Infectiousness aligns with symptom onset; therefore, close contacts need not isolate while asymptomatic. In some cases, post-exposure vaccination with modified vaccinia, Ankara vaccine (smallpox and mpox vaccine, live, non-replicating) is recommended. Contact between broken skin or mucous membranes and an infected patient's body fluids, respiratory droplets, or scabs is considered a "high risk" exposure and warrants post-exposure vaccination as soon as possible. According to the CDC, vaccination within four days of exposure may prevent disease onset, and vaccination within 14 days may reduce disease severity.

The replication-defective modified vaccinia Ankara vaccine is a two-shot series, four weeks apart, with a superior safety profile compared to first and second-generation smallpox vaccines. Unlike live vaccinia virus preparations, administering modified vaccinia, Ankara does not create a skin lesion or pose a risk of local or disseminated spread. In addition, clinical trials have shown that modified vaccinia Ankara is safe and stimulates antibody production in patients with atopy and compromised immune systems, which are known

contraindications to live vaccinia administration.

Identifying the potential benefits and drawbacks of preventative mpox vaccination in endemic communities requires more thorough data collection and feasibility analysis. Access to medical care, testing capabilities, and infrastructure limits the ability to make informed decisions about best addressing this neglected tropical disease.

Differential Diagnosis

This includes: Smallpox, Generalized vaccinia, Disseminated zoster, Chickenpox, Eczema herpeticum, Disseminated herpes simplex, Syphilis, Yaws, Scabies, Rickettsialpox, Measles, Bacterial skin infections, Drug-associated eruption

Prognosis

There are two distinct clades of the mpox virus, with a third possible clade potentially being described in the present outbreak. The West African clade has a more favorable prognosis with a case fatality rate below 1%. On the other hand, the Central Basin clade (Central African clade) is more lethal, with a case fatality rate of up to 11% in unvaccinated children. Aside from potential scarring and discoloration of the skin, the remainder of patients typically fully recover within four weeks of symptom onset.

In a cohort of 1119 confirmed cases of mpox from the ongoing outbreak in Spain, Germany, Italy, and the United Kingdom, there have been no reported deaths even though it included a subset of patients with HIV, suggesting that the circulating strain may be less virulent. However, the quality of medical care could also play a factor in this.

Complications

Bacterial superinfection of skin, Permanent skin scarring, Hyperpigmentation or hypopigmentation, Permanent corneal scarring (vision loss), Pneumonia, Dehydration (vomiting, diarrhea, decreased oral intake due to painful oral lesions, and insensible fluid loss

from widespread skin disruption), Sepsis, Encephalitis, Death

Deterrence and Patient Education

Education of patients and healthcare workers in regions where the mpox virus is endemic is of the utmost importance. Local containment is the best defense against the worldwide spread. Historically, the mpox virus has a limited ability to spread between humans. Nonetheless, the waning population of people vaccinated against smallpox paves the way for an increased prevalence of human mpox, increasing viral mutation opportunities. Therefore, improving patient recognition of this disease, reporting fidelity, and access to diagnostic capabilities are critical actions for collecting the data necessary to gain a deeper understanding of and strengthen defense against mpox.

The spread of infectious diseases requires a susceptible population and opportunities for transmission. Individual and herd immunity to mpox, previously achieved through widespread vaccinia vaccination, has declined since the 1980s, increasing human susceptibility to outbreaks. In addition, interim sociopolitical and ecological changes in endemic regions likely increased human exposure to animal reservoirs.

Due to the range of mpox disease severity, an infected patient may present to the emergency department, urgent care, or primary care setting. The ability of an interprofessional team of clinicians, nurses, virologists, veterinarians, and public health experts to promptly identify mpox infection in humans and animals, implement protective measures, and initiate public health reporting creates a bulwark against a devastating outbreak. Specialty infectious disease pharmacist consult may prove helpful in resolving the case, and in addition to infectious disease expertise, can perform medication reconciliation and counsel patients on their medications. The interprofessional paradigm will help drive better patient outcomes.

Source

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