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Monkey pox in humans: Transmission, pathophysiology, diagnosis, treatment, prevention, and all recent updates

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Abstract

The CDC is following an epidemic of monkeypox infections in the United States. Its outbreak is global now; more than 6900 cases have already been reported. There are 83 confirmed cases among children and adolescents, per the report published on November 3, 2022, in the USA. Pediatric patients are still infrequent (<0.3% of total cases). Among cases in the United States, 16 cases were in children <5 years, 12 in age group 5-12 years, and 55 cases in adolescents 13-17 years old. In the adolescent age group, 89% were male. For children <12 years of age, close physical contact with an adult household with mpox was the primary exposure, but for adolescents, male-to-male sexual contact was found more frequently. CDC advised U.S. healthcare providers to remain vigilant for patients with a rash resembling mpox, even though there is no history of travel to a country with high risk. The article here summarizes the history and epidemiology of mpox with a specific emphasis on clinical features and management in pediatric patients.

Keywords: Pediatric Monkeypox, smallpox, Monkeypox case definition, JYNNEOS Vaccine, ACAM2000

INTRODUCTION

Introduction and Background:

The monkeypox virus is an orthopoxvirus that causes mpox (monkeypox). Orthopoxviruses that infect humans range from lethal smallpox virus to highly contagious but benign molluscum contagiosum viruses ^[1]. Mpox was always found in West and Central Africa. However, in May 2022, the USA and other countries reported mpox cases, even though there was not previously documented mpox transmission. ^[2]. There are two distinct mpox virus classes: the Congo basin clade, mainly in central Africa, and the West Africa clade. ^[3]. Congo basin clade is known to cause disease with severe impact and causes more morbidity and mortality. The human-to-human transmission was also more reported with the Congo Basin clade.

Mpox in non-human primates:

Mpox virus (MPV) was first discovered in 1958 from a monkey in Copenhagen, Denmark, at the Statens Serum Institute –and that is how it got its name ^[4]; mpox virus-host also includes dormice, pouched rates, rope squirrels, and tree squirrels. Like many other zoonoses, Pox virus is found to be transmitted accidentally to a human when dealing with infected animals.

Mpox in humans:

The Dominican Republic (DR) of the Congo noted the first known human case of mpox in 1970. Six unvaccinated people from DR of Congo, Liberia, and Sierra Leone presented with an illness similar to smallpox on clinical presentation ^[5]. DR Congo reported the first pediatric case in a 9-month-old infant. Four other children from Bouduo and Liberia were also affected ages 4 to 9 years. Three children close to these cases also developed a rash the following days, pointing towards possible exposure. There was also the case of the 24-year-old male reported in Sierra Leone who reported having taken out stomach and intestine from a red monkey, and after 3-4 wk, he felt ill. No one died of mpox.

In the U.S., mpox cases were first reported in 2003 ^[6]. 71 people got infected from Gambian pouched rats and prairie dogs, as they got a shipment of these infected animals as pets. CDC and Wisconsin research department mentioned this outbreak in

which patients presented with febrile illness with vesiculopustular eruption between May and June 2003, and patients were between the ages of 3 to 43 years, out of which five were male and six female. Also, they summarized possible epidemiology, clinical, and laboratory investigations for the same outbreak. Contact with ill pet prairie dogs exposed to sick rodents from West Africa and Ghana was found in all these patients. The illness started with fever with or without chills, skin rash, and excessive sweating. All patients reported papular skin rash and headache; many reported fevers, chills, sweating, or persistent cough, and approximately half of the patients had lymphadenopathy. Characteristics rash started as a papule followed by a vesiculopustular lesion surrounded by erythema. Lesion finally resolves serous to the hemorrhagic crust with a mean duration of 12 days (3-25 days). All cases have a mild course of clinical illness, with only four hospitalized, but those also recover quickly. This is the first time mpox was identified among humans in the Western world. Only five adults were vaccinated against smallpox, while others were too young to have received it.

Nigeria had an outbreak of human mpox in 2017 ^[7]. There were 38 suspected cases, out of which 18 got laboratory confirmation, the other three were probable, and 17 didn't meet the case definition. Most of the confirmed cases were male adults. There was an association with varicella, syphilis, and HIV in two confirmed cases, and one healthcare worker had a nosocomial infection.

In September 2018, the United Kingdom reported mpox transmission from patient to healthcare worker. ^[8]. The possible source of infection was contaminated bedding. The hospital took all possible infection control measures to control the outbreak. Four of the 134 possible exposures became ill, but it was a mild clinical course.

Transmission:

Mpox infection resembles smallpox, and the illness may diagnosed earlier as smallpox was mpox because both illnesses share similar clinical features ^[9]. Mpox was found after the eradication of smallpox. Mpox is a zoonosis, although human-to-human transmission can occur. Mpox can spread from close or skin-to-skin contact. Direct

contact with mpox rash and contact with the patient's ³ saliva, upper respiratory secretions, and areas around the anus, rectum, or vagina can lead to infection. It is not very contagious as smallpox among humans. Although monkeys and other primates are the primary reservoirs, other animals, like squirrels and other rodents, can also be reservoir hosts for this virus. Pox virus DNA has been identified in anal and urethral swabs from persons who neither demonstrated clinical signs nor reported symptoms of illness at the time of specimen collection. Few cases remained asymptomatic despite having known or possible sexual exposure to infected personnel.^[10]

How Mpox relates to smallpox:

In 1980 smallpox was declared eradicated worldwide, and the last reported case was in 1977. However, Huang et al. reported that it had been over 40 years since all countries stopped giving the smallpox vaccine ^[11]. Previous history of vaccination against smallpox can give some protection with mpox, but this protection is not sure how long last. In the 2003 mpox outbreak and 2022 outbreak, multiple infected patients with mpox had a history of smallpox vaccination in past decades. ^[12]

Pathophysiology:

Mpox virus enters from routes like ¹ the oropharynx, nasopharynx, or intradermal and replicates at the inoculation site, then spreads to local lymph nodes ^[13], followed by viremia and infection to ¹ organs. The incubation period typically ranges from ⁷ to ¹⁴ days, with a maximum of 21 days. Symptoms start with fever and lymphadenopathy 1-2 days before developing skin lesions. In the 2022 outbreak, it was noted that mpox spread from when symptoms appeared to the phase where the rash had healed completely, and a new layer of skin had formed ^[14].

Case definition and Clinical features:

Below is the Case definition per CDC and *European Centre for Disease Prevention and Control* guidance ^[14,15]

Suspect Case:

New-onset typical rash

Fulfill one of the epidemiologic criteria and have a solid clinical possibility of mpox

Probable Case:

No possibility of other possible Orthopoxviral exposure (e.g., vaccination), and the evidence of the presence of

Orthopoxviral DNA by a PCR (Polymerase chain reaction) of a patient's sample OR

Orthopoxviral using immunohistochemical or electron microscopy testing methods OR

Positive anti-orthopoxviral IgM antibody after onset of rash for a duration of 4 to 56 days

Is a man who practices sex with men

Confirmed Case:

Evidence of the mpox virus detection by DNA PCR of a patient specimen or detection of virus in clinical specimen culture

Epidemiological criteria:

Within three weeks of the beginning of the illness:

Possible exposure to a person with a characteristic rash or who was diagnosed as mpox or probable case or

Intimate in-person exposure with individuals having mpox like symptoms.

Travel to a mpox endemic country outside the U.S or a country with mpox cases outbreak or

Had contact with a dead or lived wild animal or pet from an endemic African region or the product obtained from such animals.

Exclusion criteria:

Another diagnosis can be made or

An individual with high suspicious of mpox does not develop clinical symptoms or a rash within five days of illness or

High suspicious clinical specimens failed to demonstrate orthopoxvirus or antibody against it.

Clinical features:

Mpox rash begins with macules followed by papules, vesicles, and pustules. Pustules are characteristically deep-seated, firm, and well-circumscribed. These lesions can progress to umbilicate or become confluent but ultimately progress to scab.^[16] The rash can also spread to other parts of the body. But lesions on a distinct body part are in the same stage in classic monkeypox.

Classic symptomatology in mpox is fever with chills, malaise, sore throat, and lymphadenopathy, followed by a characteristic rash. However, in 2022 outbreak, there are cases where patients develop perianal and genital lesions but no fever or other systemic symptoms.

Mpox rash can mimic other common illnesses in clinical practice like syphilis, herpes simplex virus and varicella zoster, chancroid, and molluscum contagiosum, and many times, these illnesses can be associated with mpox. Therefore, it's very much required for the clinician to remain vigilant, especially with patients who present with the characteristic rash and men who practice sex with men.

Monkeypox symptoms

Treatment options

Monkeypox symptoms Treatment options: Itchy, painful pimple/blister-like rash going through several stages

Oral antihistamines, creams, and lotions like calamine lotion. Keep the rash covered, do not scratch, soaking in a warm bath, use oatmeal

Fever, chills, lymph node swelling, body ache, URI symptoms

Symptomatic pain medications

Severe disease involving eye, mouth, throat, genitals and anus

Antiviral Tecovirimat

How long is Mpox contagious?

As per ^[17], The infected person is not contagious during incubation. However, human cases can be infectious as soon as symptoms begin until all scabs from the pox lesions fall off.

Diagnosis:

Suppose there is the possibility of Mpox in the USA; the clinician should contact the health department for availability for testing, and lesions should be thoroughly swabbed and sent to testing labs. Mpox virus can be detected through an orthopoxviral PCR test at a designated laboratory, and positive PCR is enough to diagnose. Suppose complex cases or positive lab results do not meet epidemiological criteria. In that case, CDC can be consulted so that additional tests like viral-specific or clad-specific PCR and blood testing can be done.

Complications:

Reported complications are encephalitis, secondary skin infections, conjunctivitis and keratitis, and secondary pneumonia. During outbreaks in epidemic areas, mortality can be between 0% to 11%, affecting significantly young children ^[18]. Mpox severe disease is common in immunocompromised patients. Patients with HIV infection suffered more during the 2017 Nigeria outbreak, with severe skin lesions and genital ulcers, than HIV-negative patients. However, no death was reported. Between September 2017 and June 2022, Nigeria reported 257 confirmed cases, with nine deaths; out of 9 deaths, five patients were immunocompromised ^[19]. Many times, disfiguring scars and corneal damage can be significant sequelae. It's noted that vaccinated patients experienced fewer complications, and the secondary case rate in such households was lower ^[20]. As per ^[21], the pregnant patient had more complications, possibly preterm delivery, fetal death, or congenital diseases. An observational study was done at the Hospital in Koforidua between 2007 and 2011, which showed that out of four pregnant women who were included in the study with mpox, one had a Full term, healthy baby. Still, two had experienced a stillbirth in the first trimester, and one ended with fetal death.

Precautions:

It spreads from human to human *via* exposure to rashes, close contact, or things contaminated with contagious inflammation or body secretions [22]. Standard care is required for all suspected mpox patients. People with mpox who are not hospitalized require isolation at home. For confirmed Mpox, isolation must continue until all rash has healed, scabs have fallen off, and skin is intact.

Treatment:

As per [23], mpox doesn't require treatment in all patients. Immunocompromised patients, children under age eight, pregnant or breastfeeding women, with eczema or exfoliative skin lesions are considered high risk. Also, patients with severe complications or rashes involving the eyes, mouth, and private areas may qualify for treatment.

Unfortunately, there are no protocols for pediatric patients with mpox treatment, but local public health officials can always help with consultation with CDC to initiate antiviral therapy.

Tecovirimat was developed to treat smallpox, which can be used for Mpox and is currently the first-line treatment for children. The oral dose is possible for children of more than 13 kg, which can be taken as a capsule, or the capsule's content can be mixed with food. In comparison, children less than 13 kg must consider intravenous formulation depending on clinical status. Monitoring renal function is recommended, especially in children under two years of age.

CDC is also making a protocol for intravenous immunoglobulin in the case of Monkeypox, but its effectiveness is not established.

Brincidofovir was FDA-approved for smallpox treatment, and cidofovir was FDA-approved for cytomegalovirus retinitis in AIDS in the pediatric population. But still lacking data on the effectiveness of Brincidofovir and Cidofovir in treating pediatric mpox.

Post -Exposure prophylaxis (PEP):

CDC is conducting studies to determine how long immunity lasts after vaccination. They are looking at specimen samples from infected patients to see if the virus has

changed. CDC works closely with local and state partners to determine how the virus spreads among monkeypox patients. Studies have been done to find out how many patients were vaccinated if they were fully vaccinated, and when they were vaccinated. Close monitoring of people newly diagnosed with monkeypox after vaccination is ongoing.

Two vaccines can be given to people who had contact with a mpox patient [24]. Data on PEP in children are limited. JYNNEOS is the only vaccine that can be used in pediatrics. The decision must be made according to the level of risk from patients' exposure and health conditions. While vaccination is preferred in most cases, immune globulin may be considered for an infant less than six months of age. There is the possibility of using anti-viral medication after consultation with the appropriate CDC facility for PEP.

JYNNEOS:

This vaccine has not been studied well in pediatrics for mpox; it contains non-replicating vaccine virus. This vaccine has been used in pediatrics for illnesses like tuberculosis, Ebola, and measles without major side effects. In 2018-2019, this vaccine was used in the United Kingdom in pediatrics for mpox exposure without any major side effects. In the current outbreak, JYNNEOS is available for children and adolescents under 18 years of age, who are classified as high-risk exposure according to the CDC [25]. The dose would be 0.5 mL for each subcutaneous injection with two-dose series, and ideally, the first dose should be given within 96 h post-exposure.[25].

ACAM2000:

As per [26], This vaccine contains replicating viruses associated with side effects like uncontrolled viral replication and Eczema vaccinatum. It is not a preferred vaccine for pediatrics and should only be considered if JYNNEOS is unavailable or contraindicated.

Immune globulin:

Immune globulin is approved under the emergency authorization for the prevention of mpox and is preferred for infants less than six months old with high-risk exposure [27].

CONCLUSION

Mpox virus is a very contagious orthopox virus currently causing a global outbreak, primarily affecting men who have sex with men. After discontinuing the smallpox vaccine, population immunity decreased and led to increasing cases of Mpox. Furthermore, the increased number of cases outside Africa demonstrates the global spread of disease. Getting control over this infection requires doctors, hospitals, and health care officials to work together and define appropriate diagnostic testing, contact tracing, and availability of medical care to the affected patient. And is very important for pediatric physicians to make them aware of the clinical course and possible outcomes in pediatric patients. Monkeypox seems scary, but it's still a sporadic disease, especially in pediatrics. It's always good to be aware of health risks.

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