

## Household transmission of mpox

Nilo Bonifacio Morales\* <sup>1,2,a</sup>; Yuriko Yui Gómez <sup>3,4,b</sup>; Julio César Luque Espino <sup>1,c</sup>; Arturo Pareja Cruz <sup>1,d</sup>

### ABSTRACT

Mpox is a rare disease caused by the monkeypox virus (MPXV). This virus can enter the host through different routes, such as the oropharynx, nasopharynx and intradermal routes, among others. In 2022, an outbreak was reported in which the virus seemed to have mutations that would make it spread more efficiently. We present three cases of mpox in a family of eight members. Patient 1, a 32-year-old man, presented with a papule under the left eye, which was hatched manually by his wife. He then developed endophthalmitis associated with fever and headache, in addition to non-painful vesicular pruritic lesions on the extremities and genitalia. He was eventually clinically diagnosed with mpox infection. Patient 2, a 27-year-old woman (wife of Patient 1), presented with vesicular and pustular lesions on the chest, extremities and anal area six days after exposure through close contact with Patient 1. She subsequently developed myalgia, fever and odynophagia, with a positive molecular test result for MPXV. Patient 3, an 8-year-old boy, presented with odynophagia, tinnitus, fever, cervical lymphadenopathy, and umbilicated papules on the abdomen, left arm and right gluteal region seven days after the onset of symptoms in his mother (Patient 2). He also tested positive for MPXV on a molecular test. The other family members did not present clinical manifestations despite being in intrafamilial contact with the patients for approximately two weeks, during which they shared common areas and utensils without restrictions.

**Keywords:** Mpox; Antiviral Agents; Disease Prevention (Source: MeSH NLM).

### INTRODUCTION

Monkeypox virus (MPXV) is the orthopoxvirus that has most notably affected humans since the eradication of smallpox <sup>(1)</sup> and is the causative agent of this zoonotic disease <sup>(2)</sup>. It is characterized by being rare, with signs and symptoms similar to those of smallpox, but in a milder form and with a lower mortality rate <sup>(3)</sup>.

In the 20<sup>th</sup> century, mpox was mainly confined to the African continent. However, in the present century, the number of cases and the geographical spread of the disease have increased. The outbreak in several countries since May 2022 has gained significance due to an unusually high number of cases and the absence of direct links to endemic countries, which has raised concern over a possible change in the transmission pattern <sup>(4)</sup>.

Phylogenetically, the virus has two clades: one emerged from West Africa and the other in the Congo basin of Central Africa <sup>(5)</sup>. The epidemiological and clinical characteristics of the disease caused by the two clades are different. The Congo basin clade has a case fatality rate of up to 10 %, while the West African clade has a case fatality rate of only 1 %, with patients with HIV coinfection being the most affected <sup>(3)</sup>.

The first case of animal-to-human transmission was reported in 1970 in the Democratic Republic of Congo <sup>(5)</sup>. Subsequently, six cases among humans were reported in other countries, including Liberia, Nigeria and Sierra Leone, between 1970 and 1971. In Nigeria, the index case was recorded in 1971, and 10 cases were reported between 1971 and 1978. Since then, several thousand human cases have been confirmed in different countries up to the present <sup>(2)</sup>, mainly linked to international travel or the importation of African animal. It has been interesting to note that the virus isolated from the 2022 outbreak appears to have more mutations, which would be evidence of viral evolution for more efficient spread <sup>(5)</sup>.

The two possible modes of MPXV transmission are animal-to-human and human-to-human transmission <sup>(2)</sup>. The first mode occurs through scratches, bites, preparation of bushmeat or contact with bodily fluids or injured material. The second mode occurs through large respiratory droplets, sneezing, coughing, etc. Respiratory droplets do not travel long distances; therefore, prolonged face-to-face contact is necessary for transmission to occur. Other forms of human-to-human transmission include direct contact with viral lesions and bodily fluids, as

1 Universidad de San Martín de Porres, Centro de Investigación de Virología (Virology Research Center). Lima, Peru.

2 Hospital Nacional Daniel Alcides Carrión. Callao, Peru.

3 Dirección de Redes Integradas de Salud Lima Centro (DIRIS Lima Centro - Directorate of Integrated Health Networks, Lima Central Branch). Ministerio de Salud (MINSa - Ministry of Health). Lima, Peru.

4 Clínica Good Hope. Lima, Peru.

<sup>a</sup> Master in Epidemiology; <sup>b</sup> Doctor of Medicine; <sup>c</sup> Master in Clinical Research; <sup>d</sup> PhD in Medicine.

\*Corresponding author.

well as indirect contact with infected materials such as clothing or bed linens. The virus then rapidly replicates at the inoculation site and spreads to adjacent lymph nodes. Mother-to-child transmission may also occur through the placenta (congenital mpox), by close contact during and after birth. Although close physical contact is required for transmission of mpox, it is not entirely clear whether the virus can be sexually transmitted <sup>(5)</sup>.

Although smallpox virus and MPXV cause similar clinical diseases, they differ in the resulting mortality. Moreover, MPXV has a significantly lower rate of human-to-human transmission, which helps explain the epidemic potential of one virus but not the other. While the causes of the increased rate of human-to-human transmission during the most recent outbreak remain unclear, some studies suggest that as the number of people immunized with the smallpox vaccine decreases due to lack of cross-protective immunity, the risk of mpox infection increases <sup>(6)</sup>. Additionally, it is not a small fact that, in the recent outbreak, most of the cases occurred among young men who have sex with men with genital lesions that may involve close contact. Moreover, they were clearly not immunized against smallpox <sup>(3)</sup>.

The incubation period of MPXV is 12 days. Viral shedding through feces is another potential source of virus transmission. There is also evidence that household members or caregivers of a patient with mpox are at increased risk of infection; however, transmission is less efficient than that observed in smallpox <sup>(7)</sup>. Similarly, people exposed to dead game animals, pet lovers, animal husbandry facility staff, and direct contacts of patients with MPXV may be at high risk <sup>(3)</sup>.

The onset of mpox is characterized by symptoms that include fever, chills, headache, muscle aches and fatigue. These are related to a milder form of smallpox, with the difference that MPXV infection causes lymphadenopathy. The incubation period of MPXV is usually 7 to 14 days, but may take up to 21 days. After the onset of fever, the infected person develops a rash on the face, which then spreads to other parts of the body. Lesions first appear within the oropharynx and then spread throughout the body. Serum antibodies are detectable about two weeks after exposure, and the mortality rate ranges from 1 % to 10 %, depending on the infecting strain and the availability of modern medical care <sup>(5)</sup>.

The process of MPXV infection is mainly divided into two phases: the prodromal phase (lasting 0 to 2 days), characterized by fever, fatigue, severe headache, lymphadenopathy and muscle aches; and the rash phase (lasting 7 to 21 days), which appears within one to five days after fever onset and can be contagious when the rash is concentrated on the face and extremities. The rash lasts about two to four weeks and evolves from plaque

to papules, blisters, pustules and crusts before eventually shedding. Patients often present with lymphadenopathy, mainly in the groin. Mpox is a self-limiting disease, and its severity is related to the degree of exposure to the virus, the patient's health conditions and the nature of its complications. Severe cases occur more frequently in children and also lead to death, with a case fatality rate of 1 % to 10 % <sup>(3)</sup>.

Diagnostic tests are crucial in determining the presence of MPXV infection. Currently, with technological advancements, several significant tests are available, such as viral culture and isolation, immunohistochemistry, observation by electron microscopy, serological tests and conventional and real-time PCR (qPCR) tests, each using different types of specimens. The primary source of high viral load is found in skin exudates, lesion scraping or crust; on the other hand, blood, in particular, has low viral load <sup>(8,9)</sup>.

In viral culture/isolation, the specimen is cultured under aseptic conditions to isolate live virus, which allows precise categorization of viral particles and recognition of the viral effect on cells. Electron microscopy enables conventional physical observation and characterization of orthopoxviruses using negative staining. Likewise, immunohistochemical testing detects orthopoxvirus-specific antigens in biopsy specimens. Serology testing (anti-orthopoxvirus IgG, IgM), performed using immunofluorescence or neutralization assays, measures antibodies against orthopoxviruses. It is worth mentioning that it is necessary to verify whether the patient has been recently vaccinated, as this interferes with serological testing. On the other hand, conventional PCR and qPCR tests detect specific viral DNA sequences, which are exclusively used to confirm MPXV diagnosis. It is important to mention the additional genomic information, which contributes to identifying new or existing variants that are conserved in the MPXV sequences <sup>(9)</sup>.

Combining good laboratory infrastructure, trained personnel and these tests, along with clinical, epidemiological data and a patient's vaccination history, yields the best results <sup>(8)</sup>.

There are few reports of outbreaks caused by intrafamilial transmission <sup>(2,3,8,10,11)</sup>. This article describes an intrafamilial outbreak in Lima, aiming to contribute to understanding the transmission of this infection. In addition, a review of the literature is presented with updated information.

## CLINICAL CASE

We present three cases of MPXV disease within a family of eight living in an apartment in the district of San Miguel (Lima). The apartment has common areas (living room, dining room, kitchen, and bathrooms) shared by all

members and includes three bedrooms. One bedroom is used by four people: Patient 1 (the father), Patient 2 (the mother), Patient 3 (son) and Contact 1 (son). The second bedroom is shared by two young people (Contacts 2 and 3). The third bedroom is used by two older adults: Contacts 4 and 5. Family members who did not present clinical manifestations are referred to as Contacts.

The index case, referred to as Patient 1, is a 32-year-old man from Lima employed as a janitor. He is heterosexual and has no pathologic or family medical history. On July 27, 2022, he developed a papule (“pimple”) below the left eye, which was manually hatched by his wife. The following day, he presented fever for one day followed by moderate headache in the parietofrontal region, with irradiation to the ocular region of the same side, along with left ocular pain. Subsequently the patient experienced ocular pruritus, photophobia, blurred vision, lacrimation and edematous ocular congestion (Figure 1). In the following days, five non-painful vesicular pruritic lesions, compatible with mpox infection, appeared in different areas of the body (two on the right hand, one on the right forearm, one in the left malar region and one on the genitalia). As treatment, he was prescribed dicloxacillin and chlorphenamine at a healthcare facility. However, the ophthalmic discomfort persisted, and he decided to isolate himself voluntarily at home without medical monitoring. The diagnosis was made clinically, since he refused to undergo molecular confirmation testing.



**Figure 1.** Endophthalmitis in the left eye due to mpox (Patient 1)

Patient 2, a 27-year-old woman from Lima who works as a domestic worker, reported cohabiting with Patient 1. Her medical history included obesity and anemia, and she was three months postpartum. After six days of exposure through close contact with Patient 1 (manipulation of the papular lesion, sexual contact, sharing of bed linens and prolonged contact), she developed multiple vesicular and pustular lesions (Figures 2 and 3) in various areas of the body: four on the thorax, two on the abdomen, one in the oropharynx, six on the upper limbs (right and left), three on the lower limbs, and three in the anal region. In addition, the patient experienced myalgia, fever,odynophagia, and anal pain with bleeding during bowel movements. She self-medicated with paracetamol and sought medical evaluation. Following the evaluation, mpox was suspected, and a MPXV RT-PCR (real-time polymerase chain reaction for mpox) test was requested, with a positive result specific for the MPXV (INS - Instituto Nacional de Salud, Peruvian National Institute of Health]). Follow-up was performed via telemonitoring, and a subsequent home visit was conducted. Both patients shared a bedroom with their two children: an eight-year-old boy (Patient 3) and a three-month-old infant (Contact 1).



**Figure 2.** Crusted ulcerative lesion on the left lower limb due to mpox (Patient 2).



**Figure 3.** Multiple ulcerative lesions on the left upper limb due to mpox (Patient 2).

Patient 3, an 8-year-old boy and the child of the couple of Patients 1 and 2, with no comorbidities, developed symptoms seven days after his mother (Patient 2) started symptoms: odynophagia, tinnitus, fever, general malaise, cervical lymphadenopathy and, subsequently, various lesions on the neck presented as umbilicated and crusted papules. These lesions were also present in the abdominal region (Figure 4), the left arm and the right gluteal area. At the healthcare facility, he was diagnosed with pansinusitis, otomastoiditis, severe adenotonsillitis, and mpox. Consequently, he was treated with ceftriaxone and clindamycin. An MPXV RT-PCR test was requested, with a positive result specific for MPXV.



**Figure 4.** Crusted ulcerative lesion in the abdominal region due to mpox (Patient 3).

Contact 1 is a three-month-old infant, the son of Patients 1 and 2, who had close and prolonged contact with his mother. She reported not using protective measures (gown, mask, gloves), even while breastfeeding. Contact 1 never developed any clinical manifestations at any time.

For approximately two weeks, all eight family members shared common areas and utensils without restrictions. They decided to isolate Patients 1 and 2 in a room only after Patient 2 developed symptoms. Meanwhile, Patient 3, who had not yet shown symptoms, stayed in the same room as Contact 2 for four days, at which time he developed symptoms and returned to his sick parents' room, along with the infant. On the other hand, Contact 5, an older adult, left the apartment because she had diabetes.

Contacts 2, 3, 4, and 5 never developed any clinical manifestations despite prolonged intrafamilial exposure to the patients (two weeks).

## DISCUSSION

Viruses remain responsible for a large number of medically important emerging and reemerging infections. They also cause devastating diseases, and their ability to spread rapidly makes them major contributors to morbidity and mortality from infectious diseases worldwide. As the world celebrated four decades since the eradication of smallpox, Nigeria began experiencing a recent outbreak of severe skin rash syndrome that mimics a form of smallpox, with MPXV as the etiologic agent.

According to WHO, the mpox outbreak in 2022 could be another major global challenge after the challenges of the COVID-19 pandemic. As of June 10, 2022, 1,475 cases had been confirmed worldwide. Belgium was the first country to announce a three-week quarantine for mpox patients. At the onset of this outbreak, a notable number of cases was observed among men who have sex with men, a characteristic not necessarily reported in previous outbreaks<sup>(5)</sup>.

Probable causes for this outbreak in Nigeria may include a decline in herd immunity due to the cessation of smallpox vaccination, increased contact between humans and potential MPXV reservoir animals as a result of climate change and deforestation, bushmeat consumption, and inadequate health and research infrastructure, among others. These factors may have created the ecological and immunological conditions for MPXV to reemerge in Nigeria and subsequently spread. This pathogen is no longer confined to endemic regions, as travelers have exported it from Africa to the Americas, Europe and other continents in recent years<sup>(2)</sup>.

Although smallpox has been eradicated from the human population since 1980, there is a possibility that mpox could fill this gap <sup>(12)</sup>. Although MPXV has relatively low infectivity and may not evolve into a pandemic, the 2022 outbreak was the largest and most widespread MPXV epidemic outside Africa up to that time. Consequently, this international outbreak has raised alarms among international health authorities <sup>(3)</sup>.

It is impossible not to question whether the current outbreak reflects a new transmission pattern for MPXV or whether the virus has mutated or has the potential to mutate to become more transmissible to humans. While this outbreak may have taken most of the world by surprise, mpox has been reemerging in Africa for more than 20 years. Also, some of its characteristics are unusual, including sustained human-to-human transmission among men who have sex with men, which requires thorough study to understand whether a new transmission pattern has emerged. In this post-COVID and more vigilant world, understanding the biology and ecology of the poxvirus family is becoming increasingly important <sup>(4)</sup>.

In terms of cases in the core family, in May 2021, three members of a family who returned to the United Kingdom after traveling to Nigeria became infected with MPXV. Secondary transmission from the index case occurred within the family, to another adult and a young child. The concurrent control measures associated with COVID-19 facilitated detection and limited the number of potential contacts <sup>(13)</sup>.

Bellido et al. <sup>(10)</sup> reported a familial outbreak of household mpox from an adult male to a 10-month-old infant. The index case lived with his wife and two daughters—one 2.5 years old and the infant—but neither the wife nor the older daughter had symptoms. The index case and the infant developed symptoms related to mpox infection, which was confirmed by PCR. The wife and older daughter had late oropharyngeal swab PCR testing, with negative results for both cases. The infant was exclusively breastfed. The authors indicated that transmission may have occurred due to the father's failure to adhere to adequate isolation measures or through the mother, who may have had an asymptomatic infection. Alonso-Cadenas et al. <sup>(14)</sup> described a case of transmission to a seven-month-old infant from the mother, who had lesions on the chest.

Besombes et al. <sup>(11)</sup> described a family transmission outbreak in the Central African Republic in 2018. The index case probably acquired the infection through contact with wild animals (killed three small mammals identified as a civet, a rat, and a squirrel). He then transmitted the disease to his two daughters (aged 5 months and four years), as well as to two of his sisters (aged 7 and 16 years), his 33-year-old sister-in-law, and his mother (asymptomatic).

PCR testing confirmed the presence of the MPXV in his symptomatic relatives. On the other hand, the mother of the index case tested positive for serology, as did one of his brothers, who brought the wild animals to her, and two healthcare workers who attended him. The authors reported that transmission occurred in three waves of intrafamilial infection.

Regarding household transmission in this report, the index case (the father) mentioned that there was a person with skin lesions and fever in the building where he worked as a janitor. Therefore, he suspects that it could have been mpox, although he did not have direct contact, only indirect contact through touching door handles. The transmission of the infection in this family is noteworthy, since there was a long period—up to three weeks—of intra-household contact in which all the members (eight people) shared utensils, household items and bathrooms before the isolation of those who became ill. Nonetheless, only three of them developed the disease. Unlike the rest of the family members, these patients had close contact, as they slept in the same room. However, an infant who also stayed in the room did not become ill, despite having close contact with his mother during breastfeeding, which occurred without protective measures (gloves, mask or gown). The instructions for strict isolation of the father and the other sick people at home were difficult to follow due to the housing conditions (small, old and poorly ventilated). At that time, it was not possible to test the other family members for this virus due to the unavailability of such tests. In addition, it was not possible to confirm the infection of the index case due to the patient's refusal, although the infection of Patient 2 (the mother) and Patient 3 (son) was confirmed through molecular testing. It was not possible to perform molecular or serological tests on the infant, who remained asymptomatic.

Based on current knowledge, we could state that the infant was probably infected through close and intimate contact with the mother but did not develop the disease. Regarding the other family members who did not develop the disease, we cannot establish whether they were infected or not. However, since they did not have intimate contact, they were probably not infected. Nevertheless, there is the possibility of infection through airborne transmission or contaminated surfaces, since a study <sup>(15)</sup> found replication-competent concentrations of the virus in the air and on the floor of the room occupied by the patient with MPXV infection, suggesting the possibility of infection, although with low probability.

MPXV has been detected in multiple lesions, mucous membranes, secretions and excretions of infected and/or sick people, as well as in fomites, although the ability to transmit the infection depends on the viral load in the reservoir and not only on the presence of the virus. The

updated studies and research provide further clarification on the transmission of MPXV, as described by the Centers for Disease Control and Prevention (CDC) in their Scientific Brief: Detection and Transmission of Mpox (Formerly Monkeypox) Virus During the 2022 Clade IIb Outbreak (updated February 2, 2023). Replication-competent (i.e., potentially infectious) viral concentrations have been detected in the following samples: skin lesion swabs (blisters and ulcers), oropharyngeal swabs, anorectal swabs, urethral swabs, as well as in conjunctivae, semen and vaginal discharge <sup>(16)</sup>.

MPXV has been detected by PCR in swabs from conjunctival tissues or eyelid lesions and in the corneal epithelium of patients with ocular infection caused by this virus <sup>(17,18)</sup>. In one case with conjunctivitis, replication-competent virus was detected, but without lesion <sup>(19)</sup>. Therefore, exposure to conjunctivae or ocular fluids could transmit the infection, particularly in the presence of conjunctivitis.

On the other hand, low concentrations of non-replication-competent virus have been detected in urine samples. No cases of transmission with epidemiological link to urine exposure have been reported; however, it has been determined that this fluid could transmit the infection <sup>(20,21)</sup>. The virus has also been identified in blood (plasma and serum), but at low, non-replication-competent concentrations <sup>(20,22)</sup>. The virus has also been detected in feces, but at non-replication-competent concentrations, and no epidemiological link has been observed <sup>(23,24)</sup>. There are no data to support that breastfeeding is a source of infection <sup>(16)</sup>.

Intrahospital transmission has been reported among healthcare personnel who have had contact with sharp instruments used for specimen collection from skin lesions <sup>(25,26)</sup>. Outside the hospital setting, the virus has been found on equipment used for tattooing and piercing, which could be a source of transmission if used after being contaminated by source patients <sup>(27,28)</sup>.

MPXV DNA has been detected at low levels in samples from some individuals who never developed symptoms. Nevertheless, there is currently no evidence that these individuals are infectious or can transmit the virus to others <sup>(16)</sup>. Individuals infected with MPXV can transmit the virus before the onset of signs and symptoms of the disease <sup>(29,30)</sup>, a period ranging from one to four days <sup>(31)</sup>.

Virus DNA has also been detected in anorectal, urethral, genital and oropharyngeal swabs, as well as in the saliva of exposed individuals who never developed symptoms, although in low concentrations near the detection limit of the test. Therefore, it was not possible to conduct tests for replication-competent virus <sup>(16)</sup>.

Although widespread surface contamination with MPXV has been detected in homes and hospital rooms of patients with symptomatic mpox, the concentrations were low on both surfaces and in air samples <sup>(16)</sup>. In a study of hospital patient isolation rooms, culturable virus was found on gloves used to examine patients, the soap dispenser lever in a patient's bathroom, and a towel on one patient's bed <sup>(32)</sup>.

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NBM and YYG were responsible for the conception of the article; NBM and JLE for literature search; YYG and NBM for patient evaluation; NBM and JLE for writing; and NBM and APC for the article revision.

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**Corresponding author:**

Nilio Bonifacio Morales

Address: Av. Simón Bolívar 937, Pueblo Libre. Lima, Perú

Telephone: 4602366

E-mail: nbonifacio@usmp.pe

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**ORCID iDs**

Nilio Bonifacio Morales

 <https://orcid.org/0000-0002-8624-0181>

Yuriko Yui Gómez

 <https://orcid.org/0000-0001-9763-1746>

Julio César Luque Espino

 <https://orcid.org/0000-0001-8868-2883>

Arturo Pareja Cruz

 <https://orcid.org/0000-0002-5988-5515>