



Pathogen

Monkeypox virus (MPXV) is a double-stranded DNA virus belonging to the Orthopoxvirus genus, Poxviridae family. It is closely related to the variola virus (smallpox), cowpox virus and the vaccine virus. Historically, there have been two clades of MPXV - clade I in Central Africa (formerly the Congo Basin clade) and clade II in West Africa.

Mpox is not a new virus. It has been known to infect humans since the 1970s. It was formerly known as monkeypox because it was first discovered in infected monkeys. Nowadays, we know that monkeys are not the natural reservoir but accidental hosts like humans. The name was changed to mpox in 2022.

Occurrence | Risk areas

Mpox has been commonly found in West and Central Africa where the suspected natural reservoir is endemic. Since the end of smallpox vaccination campaigns in the early 1980's, cases of mpox have increased, slowly at first and significantly in the last 5-10 years, especially in the Democratic Republic of Congo (DRC).

In 2022, a new emerging clade IIb was responsible for a global epidemic that spreads mainly through sexual contact, among men who have sex with men. It resulted in the first public health emergency of international concern (PHEIC) declared by the WHO (ended in May 2023). Although the clade IIb epidemic is now under control, the clade continues to circulate worldwide (see ECDC 2022 and WHO pages).

In 2024, the continued increase of mpox clade I cases in endemic regions of Central Africa, especially in the DRC, and the emergence of a new clade Ib in Eastern DRC and neighboring countries have raised global concern and prompted the WHO to declare a PHEIC for the second time in two years. The clade Ib has emerged outside the known endemic regions of DRC, affecting the eastern part of the DRC and neighboring countries through sexual networks involving sexual workers and their clients and is now also spreading further within households and other settings (see ECDC 2024 and WHO pages).

In Switzerland

Since the 2022 outbreak, sporadic cases of clade IIb have been diagnosed in the country linked to sexual exposure, mainly among men who have sex with men. At present, imported cases are likely to occur with either of clade IIb or the new clades Ib. However, the risk for the local population is minimal. Likewise, the risk to travelers is considered very low if general precautions (see below) are followed.

Source / Reservoir

The natural reservoirs of mpox are thought to be small mammals in the endemic region of Africa, in particular the African squirrel species: redshank squirrels (and possibly others *Funisciurus* and *Heliosciurus ssp.*) and rats. Monkeys, like humans, are accidental hosts.

Transmission

Animal to human: Mpox can spread from animal to human when they come into close contact with an infected animal (rodents or primates) including through bites, secretions, excretions and consumption of insufficiently heated meat of infected animals ("bushmeat").

Human to human: Mpox can spread from person to person through close physical contact (sexual or non-sexual) with someone who has symptoms of mpox. The cutaneous and mucosal lesions, body fluids (such as fluid, pus, or blood from skin lesions), and scabs are particularly infectious. A person can also be infected through touching or handling clothing, bedding, towels, or objects like eating utensils/dishes that have been contaminated by contact with a person with symptoms. Ulcers, lesions, or sores in the mouth can also be infectious, meaning the virus can spread be through saliva. MPXV can also be transmitted vertically during pregnancy. Household members, family caretakers, and sexual partners of a confirmed case of mpox are at higher risk for infection as are health workers who treat a case without adequate personal protection.

It is not clear whether people who do not have symptoms can transmit the disease.

Incubation period

3-21 days, average 6-13 days.





Disease

The clinical picture is similar to that of variola infection (smallpox), although the overall course is significantly milder. The disease caused by clade IIb as a case fatality rate of less than 0.2%, while the disease caused by the clade I has a case fatality around 4%. The case fatality of clade Ib is not yet known.

Initial symptoms include a prodromal phase with:

• fever, headache, muscle aches, back pain, and often marked lymphadenopathy.

One to three days after the onset of symptoms, the typical, sometimes painful rash / eruptions appear:

- It passes through several stages (macules → papules → vesicles → pustules → crusts).
- The rash is usually concentrated on the face, palms, and soles.
- Mucous membranes (enoral, ocular, genital, anal) may also be involved.
- Lesions may be isolated to the genital area or be disseminated; there may be a few or hundreds of lesions, and fever may be absent.
- Lesions heal with scarring after the crust falls off.

The disease lasts 2-4 weeks.

Differential diagnosis should be made between chickenpox and secondary syphilis (during the macular and papular phase of mpox). In contrast to chickenpox, mpox skin lesions appear all at once and progress together through the different stages (in chickenpox, different stages of efflorescence occur at the same time, so-called "starry sky").

Complications include secondary bacterial infections, pneumonia, encephalitis, keratitis and corneal ulceration, sepsis, and dehydration and malnutrition. Lack of access to health care (supportive) in certain regions of Africa increases the risk of complication. Rarely, people may present with severe systemic forms with multiorgan involvement. Children, pregnant women and people with weakened immune systems are most at risk of suffering complications.

Duration of contagiousness

Transmission is possible throughout the duration of the disease until the lesions are completely healed and the crust falls off, usually 2 to 4 weeks.

Diagnosis

By clinical features and virological confirmation: analysis of vesicular fluid or crust by real-time PCR GeneXpert or other antigenbased rapid diagnostic tests. Serology has no role in diagnosis of acute infection.

Specialist laboratories that offer above virological analyses: Reference laboratory for emerging viral diseases (<u>CRIVE – HUG</u>) or the <u>Spiez Laboratory</u> or the ZBS1 at the Robert Koch Institute (RKI; <u>consiliary laboratory for smallpox</u>)

Treatment

Primarily symptomatic to alleviate symptoms (e.g., pain) and prevent complications. An oral antiviral drug (Tecovirimat, TPOXX®) is approved as treatment in the USA (mechanism of action: inhibits virus release from infected cells), but shows only limited benefits. The intravenous form is reserved for severe cases (still under evaluation at the FDA). Cidofovir (i.v.) also has activity against MPXV, but is complex to administer (nephrotoxicity!). In Switzerland, tecovirimat is under study and can be used in the context of trials or in specific clinical situation based on the guidance from the National Medical Societies.

In in case of symptoms:

- Reporting of mpox cases is mandatory! Notification formulary, see <u>FOPH LINK.</u>
- Patients should stay at home (self-isolation) until mpox rash has healed and a new layer of skin has formed. Staying away from other people and not sharing personal items with others will help prevent the spread of mpox.
- People with mpox should regularly clean and disinfect the spaces they use to limit household contamination.
- No sex while symptomatic and while lesions are present.
- Condoms should be used for 12 weeks after infection.



Expertenkomitee für Reisemedizin Comité d'experts pour la médecine des voyages Comitato di esperti per la medicina di viaggio Expert committee for travel medicine

Prevention

General precautions:

- · Worldwide:
 - ✓ avoid close, skin-to-skin contact with people who have or may have mpox or people who have a rash (e.g., pimples, blisters, scabs).
 - ✓ Wash your hands often with soap and water or an alcohol-based hand sanitiser containing at least 60% alcohol.
 - ✓ Avoid touching potentially contaminated personal items such as bedding/clothing, towels or sharing eating utensils/cups, food or drink with a person who has, or may have mpox.
 - ✓ Avoid sex with sick persons; use of condoms for up to 12 weeks if your sexual partner had mpox.
 - ✓ Follow advice of local authorities.
- When travelling to endemic / epidemic areas in Africa, in addition to above mentioned general precautions:
 - ✓ Avoid contact with wild animals in areas where mpox regularly occurs.
 - ✓ Avoid eating or preparing meat from wild animals (bushmeat) or using products (creams, lotions, powders) derived from wild animals.

Vaccination:

Three vaccines are available worldwide:

- MVA-BN (Jynneos®, Imvanex®, Imvamune®, manufactured by Bavarian Nordic), is a live attenuated, non-replicating vaccine (based on the vaccinia virus) with a two doses regimen. It is approved by the US Food and Drug Administration (FDA), the European Medicines Agencies (EMA) and Swissmedic. It is used in many countries and has a good safety profile (third generation). Vaccination effectiveness after 2 doses is estimated to be 66-86% in high-risk cohorts (76% after one dose).
- ACAM2000®, is a replicating-competent vaccinia virus vaccine; approved for emergency use in some countries, significant side-effects (second generation).
- LC16 (KM Biologics, Japan), is an attenuated smallpox vaccine, licensed in Japan.

The vaccines were initially developed to fight against smallpox but offer a cross protection against mpox.

Indication for vaccination:

- Groups at risk (e.g., men who have sex with men or transgender person, with multiple sex partners, laboratory workers handling mpox virus) are eligible for vaccination since 2022 and this recommendation remains unchanged.
- In light of the current epidemiological situation in Africa in 2024, the Swiss Expert Committee for Travel Medicine recommends vaccination against mpox for (recommendation as of 27 August 2024, updates see news):
 - ✓ professionals who are / will be in contact with suspect mpox patients or MPXV in endemic/epidemic regions (clinical or research work) or working with animals
 - ✓ post-exposition prophylaxis (PEP) in the event of a high risk exposition (health care workers or contact persons). The effectiveness of PEP is low and is estimated at 20%.

The vaccination is currently **not** recommended for travelers who do not fulfill the above-mentioned indications.

References, literature and websites

- Federal Office of Public Health Switzerland, monkeypox
- Spiez Laboratory, LINK
- Reference Laboratory for Imported Viral Diseases (HUG)
- European CDC, monkeypox
- WHO, monkeypox
- WHO, mpox dashboard (see cases and deaths global trends)
- CDC, monkeypox
- ESCMID: Activities
- Mpox in people with advanced HIV infection: a global case series. The Lancet, February 21, 2023. https://doi.org/10.1016/ S0140-6736(23)00273-8
- Bunge EM et al. The changing epidemiology of human monkeypox A potential threat? A systematic review. PLoS Neglected Tropical Disease, February 11, 2022. https://doi.org/10.1371/journal.pntd.0010141
- Mpox is there a more dangerous new clade? Christian Hoffmann. The Lancet Infectious Diseases, 28 August 2024: https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(24)00564-4/fulltext
- Sustained human outbreak of a new MPXV clade I lineage in eastern Democratic Republic of the Congo. Nature Medicine 2024: https://www.nature.com/articles/s41591-024-03130-3