Monkeys

Monkeypox Virus – Interim Fact Sheet

Disease Agent:

- Monkeypox virus (MPXV)

Disease Agent Characteristics:

- Family: Poxviridae; Subfamily: Chordopoxvirinae; Genus: Orthopoxvirus
- Virion morphology and size: Enveloped, slightly pleomorphic; dumbbell-shaped core with lateral bodies; 140-260 nm in diameter by 220-450 nm in length
- Nucleic acid: linear, double-stranded DNA virus; genome length: ~197 kb in length bp
- Physicochemical properties: Resistant to common phenolic disinfectants; inactivated with polar lipophilic solvents, such as chloroform, and at low pH. Complete inactivation of the closely related vaccinia virus occurs in 2-3 hours at 60°C or within minutes following exposure to 20 nM caprylate at 22°C; however, MPXV is more resistant than vaccinia to solvent-detergent treatment.

Disease Name:

- Monkeypox

Priority Level:

- Scientific/Epidemiologic evidence regarding blood safety: Theoretical
- Public perception and/or regulatory concern regarding blood safety: Very low
- Public concern regarding disease agent: Low to very low at time of 2003 United States (US) outbreak and 2021 imported US cases. Increasing public concern with the 2022 outbreak.
- An international outbreak is in its early stages (June 2022). On July 23, 2022, the director general of the WHO declared the current epidemic a public health emergency of international concern under the International Health Regulations.

Background:

- 1958—MPXV first identified in laboratory monkeys at State Serum Institute in Copenhagen
- 1970—First human case of MPXV detected in Zaire (Democratic Republic of the Congo— DRC) after smallpox eradication in the country
- June 2003—First case of MPXV in Western Hemisphere was in the US. The source of this single outbreak was Gambian pouched rats imported from West Africa. Prairie dogs housed in pet stores in close proximity to these became infected and transmitted the infection to humans.
- July 2021—imported case of monkeypox diagnosed in Dallas, Texas in returning traveler from Nigeria. No subsequent transmission documented.
- Other members of the Orthopox genus include variola virus (smallpox virus), vaccinia virus (smallpox vaccine virus), ectromelia virus, camelpox virus, and cowpox virus.
- Two clades are recognized and have been renamed during the 2022 global epidemic:
  - The Central African (Congo Basin) clade present in Gabon, Cameroon, Republic of Congo, Central African Republic, and the Democratic Republic of Congo is now designated clade I.
The West African clade, less virulent than clade I, is present in Nigeria, Sierra Leone, Ivory Coast, Liberia, and the US (ex-Ghana) during the 2003 outbreak is designated clade IIa.

The 2022 international outbreak is caused by clade IIb.

**Common Human Exposure Routes:**

- Animal to human transmission occurs by a bite, scratch, direct contact with body fluids or lesion material or indirect contact (e.g., contaminated bedding) or through preparation and/or consumption of bushmeat.
- Human-to-human transmission is thought to occur primarily through direct (i.e., skin-to-skin) contact, including that associated with sexual activity during the 2022 outbreak. Contamination of the inanimate environment, esp. clothing and linens, with virus from skin lesions can also occur, particularly among caregivers. Large respiratory droplets after prolonged face-to-face contact may transmit.
- The 2022 international outbreak includes a predominance of infection of men who have sex with men (MSM) although it has not traditionally been considered a sexually transmitted infection. Semen harbors MPXV DNA and infectious virus in a proportion of cases.

**Likelihood of Secondary Transmission:**

- Before 2022, the risk of human-to-human transmission was considered low, but the 2022 outbreak appears to be driven by direct contact with an infected patient.
- Droplet transmission requires prolonged face-to-face contact (e.g., within a 6-foot radius for >3 hours) but does not appear to be a major route of transmission.
- Extent of exposure (e.g., complex bite wound vs simple touching) can influence disease severity.
- Period of human-to-human transmission is from the onset of symptoms until scabs are dry, separated and lesions epithelialized. It remains unclear if transmission can occur prior to the appearance of symptoms.

**At-Risk Populations:**

- Historically, risk was very low outside endemic areas, based on animal import controls.
- The extent of transmission with the 2022 outbreak remains to be fully characterized, is currently concentrated in MSM sexual networks in which multiple and anonymous contacts are common but may extend to other cohorts as the epidemic evolves.
- In Africa, people coming in contact with infected animals including bushmeat

**Vector and Reservoir Involved:**

- Reservoir is unknown but suspected to be African rodents
  - Animal vectors include rodents and squirrels. All mammals are considered potentially susceptible to infection. Despite its name, monkeys are not considered an important reservoir.
  - The potential for establishment of an animal reservoir(s) in historically nonendemic countries is an important concern during the 2022 epidemic.
Blood Phase:

- In a 2003 outbreak in the Republic of Congo, 2 of 3 peripheral blood samples from 3 probable/confirmed patients were DNA PCR positive (1 of 5 samples positive on day 33 after rash onset). Among US samples from 2003, 3 of 12 were positive and one was equivocal within 21 days of rash onset; none were positive/equivocal beyond 21 days after onset.
- Among 7 patients in the UK between 2018 and 2021, 6 of 7 had a positive blood PCR at some point after rash onset, with the latest detected at day 30 after onset.
- Animal models demonstrate infectious viremia and parenteral transmission in non-human primates.
- Asymptomatic infectious viremia has not been well studied.

Survival/Persistence in Blood Products:

- Unknown

Transmission by Blood Transfusion:

- No cases have been documented.
- Parenteral transmission has been demonstrated in animal models.

Cases/Frequency in Population:

- Precise surveillance is not available but in a Nigerian outbreak since 2017 there have been 200 confirmed cases with 500 suspected.
- Sporadic outbreaks have occurred in other Central and West African countries usually close to tropical rain forests where humans have frequent contact with infected animals.
- The 2003 outbreak in the US, as a result of virus introduction through infected exotic pets, resulted in 47 laboratory-confirmed cases.
- As of 31 Aug 2022, 51,267 cases were reported globally including 18,989 from the US. As of 31 Aug 2022, several countries have reported decreasing infection rates likely due to the implementation of public health measures.

Incubation Period:

- 6-13 days (mean of 12 days, range of 5-21)

Likelihood of Clinical Disease:

- A high percentage of exposed individuals develop clinical disease.
- In addition, serological evidence of infection has been reported in about 3% of asymptomatic household contacts of MPXV symptomatic individuals studied between 1980 and 1984 in the DRC.
  - Asymptomatic infection has been reported from the EU during the 2022 epidemic, but its extent and any association with infectious viremia is not yet characterized.

Primary Disease Symptoms:
Most patients demonstrate characteristic prodromal illness for 2 days before the onset of rash with fever, malaise, and lymphadenopathy. The prodrome may be milder and even absent among infections during the 2022 outbreak.

Many patients infected with monkeypox develop lymphadenopathy, which is a key feature distinguishing human monkeypox from smallpox.

Typical monkeypox rash, which can be intensely painful, begins as maculopapular lesions of 2-5 mm in diameter; the rash becomes generalized in distribution in most cases, spreading in centrifugal pattern although more limited skin disease appears to be a feature of the 2022 epidemic.

Skin lesions progress from macules to papules to firm, deep seated vesicles and pustules followed by umbilication, scabbing, and desquamation over a period of 14-21 days.

Lesions are observed on mucous membranes, including the mouth, on the tongue, and on genitalia.

Lesions in atypical locations are prominent during the 2022 outbreak, e.g., the genital skin and anorectal mucosa.

Severity of Clinical Disease:

In addition to skin lesions, extracutaneous manifestations, such as secondary skin and/or soft-tissue infection (19% of cases), pneumonitis (12%), ocular complications (4%-5%), and encephalitis (<1%), are also observed.

No hemorrhagic form of monkeypox has been described in humans.

Among individuals with smallpox vaccination history, the rash is milder and more likely to be pleomorphic.

Pediatric and immunocompromised patients are more likely to suffer severe infection and complications.

A high proportion of 2022 cases are in HIV-infected patients, but the illness does not seem more severe if HIV is well managed with antiretroviral therapy.

Mortality:

In Africa, the reported mortality rate differs between clades I and II.

Clade IIa has a case fatality rate of 1-3.6% vs. 10.6% for clade I. This compares to a 30% mortality with smallpox.

- Reported mortality in locales with access to advanced medical care is substantially lower.
- Mortality during 2022 from the IIb strain is much lower than historic case fatality rates in endemic countries.

Chronic Carriage:

Not recognized

Treatment Available/Efficacious:

Preexposure immunization may be recommended for individuals with a very high risk of exposure to MPXV including high-risk cohorts and laboratory workers.

No proven treatment for humans but animal studies suggest effectiveness with tecovirimat, that has been approved for treatment of smallpox.
It has protected nonhuman primates from fatal monkeypox virus infection. Limited supplies are available in the U.S. Strategic National Stockpile and available under IND. Availability elsewhere may be limited or non-existent.

- Cidofovir and brincidofovir (used to treat serious CMV infections) have in vitro activity but lack clinical data.

- In animals, treatment with antiviral compounds is more effective in reducing mortality than the therapeutic use of smallpox vaccine.
  - Postexposure immunization with vaccinia vaccines may be effective for monkeypox prevention or mitigation of disease severity and is recommended for high-risk, exposed individuals.

- Data are not available on the effectiveness of vaccinia immune globulin (VIG) for treatment of monkeypox complications. It is administered under an IND and but has no proven benefit in the treatment of smallpox complications. It is unknown whether a person with severe monkeypox infection will benefit from treatment with VIG, however, its use may be considered in such instances.
  - VIG can be considered for prophylactic use in an exposed person with severe immunodeficiency in T-cell function for which smallpox vaccination following exposure to monkeypox is contraindicated.

**Agent-Specific Screening Question(s):**

- No specific question is in use.
- Not indicated because transfusion transmission has not been demonstrated.
- No sensitive or specific question is feasible.

**Laboratory Test(s) Available:**

- No FDA-licensed blood donor screening test exists; however, research-based NAT assays are in development.
- A PCR-based algorithm is in diagnostic use for the 2022 outbreak. Confirmation of monkeypox infection is based on detection of unique sequences of MPXV viral DNA. If a MPXV specific test (preferable) is not available, an orthopoxvirus-positive PCR can be considered confirmation in non-endemic countries. PCR can be used alone, or in combination with sequencing.
- Serological tests are not useful for the diagnosis of acute infection.

**Currently Recommended Donor Deferral Period:**

- No FDA Guidance or AABB Standard exists.
- Prudent practice would be to defer infected donors at least until all lesions are fully resolved and a minimum of 21 days after the onset of symptoms.
- Based on the incubation period, CDC has recommended that asymptomatic close contacts of infected people or animals be placed under fever surveillance for 21 days. The 21 days would be a minimum donor deferral if such contact has occurred.
- The need for specific interventions to minimize a theoretical risk of transfusion transmission of MPXV during the unique 2022 epidemic is undetermined.
Donors must be well on the day of donation, undergo a limited skin examination, and have their temperature taken in the donor room.

In the US, MSM are specifically deferred for three months after the most recent such contact to reduce the risk of collecting donations from recently HIV-infected donors. This interval is believed to be well beyond the duration of a putative MPXV infectious viremia and high adherence to this donor criterion effectively mitigates any risk where donors continue to be directly questioned about MSM activity.

In much of the world, the MSM deferral has been discarded and replaced by individual donor risk assessments. These recognize the importance of behaviors, as opposed to sexual preference, in disease transmission risk, e.g., multiple recent and new sex partners and traumatic sexual practices. In the context of the current epidemiology of the outbreak, overwhelmingly affecting MSM, it may be necessary in such venues to add specific inquiries regarding potential exposures to MPXV, as has been recommended by the European Centers for Disease Control.

Impact on Blood Availability:
- Agent-specific health question(s): Not applicable
- Laboratory test(s) available: Not applicable

Impact on Blood Safety:
- Agent-specific screening question(s): Not applicable
- Laboratory test(s) available: Not applicable

Leukoreduction Efficacy:
- Unknown

Pathogen Reduction Efficacy for Plasma Derivatives:
- Multiple pathogen reduction steps used in the fractionation process have been shown to be robust in removal of enveloped viruses.
- Pasteurization has been effectively used for inactivation of vaccinia virus and may be useful for monkeypox. In contrast, vaccinia virus was relatively resistant to inactivation by solvent/detergent treatment of blood products.
- Nanofiltration of plasma may be effective in the removal of monkeypox virus.

Other Prevention Measures:
- Avoidance of contact with potential animal sources, infected patients and contaminated materials (e.g., bedding), careful hand hygiene and personal protective equipment are key.
- Extensive DNA sequence and amino acid homology among poxviruses give rise to cross-immunity against various poxviruses, explaining a protective effect of vaccinia virus vaccines used for smallpox for monkeypox. With the eradication of smallpox and the cessation of near-universal vaccination,
population immunity has likely declined in younger age cohorts and susceptibility to monkeypox may be increasing.

- A very safe attenuated, replication-deficient, live virus vaccinia vaccine (JYNNEOS™) may be very effective in preventing human monkeypox disease. It is FDA-approved for pre-exposure monkeypox prevention and CDC recommends its use for exposed people up to 14 days after the exposure. Historic data from Africa suggest it is at least 85% effective, preventing illness when administered within 4 days of exposure and may ameliorate symptoms after infection when given beyond that window.

- ACAM-2000, an attenuated, replication-competent vaccinia-based smallpox vaccine, is also available in the national stockpile but side effects and secondary transmission to immune-compromised individuals are more likely than with the replication-deficient JYNNEOS and would be useful only for contacts with contraindications to JYNNEOS.

- Donor room infection control
  - Risk in donor rooms should be minimal given the requirement for intimate and prolonged contact for transmission
    - Donors must be healthy
    - Fully clothed
    - Afebrile
    - Routine cleaning procedures should be sufficient
  - Infected collection facility personnel should follow public health recommendations for isolation and quarantine.
  - Potentially exposed collection facility personnel may continue to work as long as they remain asymptomatic.

Other Comments

- Waning immunity after the discontinuation of routine smallpox vaccination may lead to concern that MPXV might be used as a bioweapon.

Suggested Reading:


