Monkeypox Virus

Disease Agent:

- Monkeypox virus (MPV)

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, MPV 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: Absent but very low at time of 2003 outbreak
- Public concern regarding disease agent: Absent but very low at time of 2003 outbreak

Background:

- 1958—MPV first identified in laboratory monkeys at State Serum Institute in Copenhagen
- 1970—First human case of MPV detected in Zaire (Democratic Republic of the Congo—DRC) after smallpox eradication in the country
- June 2003—First case of MPV in Western Hemisphere was in the US. The source of this single outbreak was small mammals imported from West Africa. Prairie dogs housed in pet stores in close proximity to these infected small mammals became infected and transmitted the infection to humans.
- 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: 1) The Congo Basin clade present in Gabon, Cameroon, Congo Basin Nation RCG, and DRC; 2) The Central African clade present in Nigeria, Liberia, and the US (ex-Ghana). The West African clade is less virulent than the Congo Basin clade.

Common Human Exposure Routes:

- Respiratory, percutaneous, and permucosal exposures to infected monkeys, zoo animals, prairie dogs, and humans

Likelihood of Secondary Transmission:

- Direct contact with body fluids, respiratory droplets, or with virus-contaminated objects, such as bedding or clothing
- Period of human-to-human transmission is during the first week of the rash.
- Longest chain of documented human-to-human transmission was five generations (four serial transmissions).

At-Risk Populations:

- Very low in the US, based on animal import controls established in 2003
- In Africa, people coming in contact with infected animals

Vector and Reservoir Involved:

- Reservoir is African rodents

Blood Phase:

- In an outbreak in the Republic of Congo, one out of five specimens was positive after 21 days. In a concurrent US outbreak, all 14 blood specimens collected 21 days after the appearance of rash were negative for MPV DNA.
- Asymptomatic viremia has not been well studied.

Survival/Persistence in Blood Products:

- Unknown

Transmission by Blood Transfusion:

- No cases have been documented.

Cases/Frequency in Population:

- Several documented outbreaks have occurred in Central and West Africa 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 37 laboratory-confirmed cases. No cases have been reported in the US since that outbreak.

Incubation Period:

- 7-17 days (mean of 12 days)

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 MPV symptomatic individuals studied between 1980 and 1984 in DRC.

Primary Disease Symptoms:

- Most patients demonstrate characteristic prodromal illness for 2 days before the onset of rash with fever, malaise, and lymphadenopathy.
- Almost 90% of patients infected with monkeypox develop lymphadenopathy, which is the key feature distinguishing human monkeypox from smallpox.
- Typical monkeypox rash begins as maculopapular lesions of 2-5 mm in diameter; the rash becomes generalized in distribution in most cases, spreading in centrifugal pattern.
- Skin lesions progress from papules to vesicles, and pustules followed by umbilication, scabbing, and desquamation over a period of 14-21 days.
- Skin lesions are observed on mucous membrane, in the mouth, on tongue, and on genitalia.

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 patients are more likely to be hospitalized in an intensive care unit.

Mortality:

- In Africa, the reported mortality rate is about 10% among patients with disease.

Chronic Carriage:

- No

Treatment Available/Efficacious:

- No proven treatment for humans but animal studies show effectiveness of antiviral treatment either with cidofovir or with a related acyclic nucleoside phosphonate analog.
- In animals, treatment with antiviral compounds is more effective in reducing mortality than the therapeutic use of smallpox vaccine.

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.
- Currently, CDC uses cell culture or chick chorioallantoic membrane isolation in conjunction with a DNA-based assay for the diagnosis of orthopox virus infection.
- Several DNA-based tests and sequencing are useful.
- 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 donors at least until signs and symptoms are gone or 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 deferral if such contact has occurred.

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.
- Treatment with solvent-detergent and pasteurization has been effectively used for inactivation of vaccinia virus and may be useful for monkeypox.
- Nanofiltration of plasma may be effective in the removal of monkeypox virus.

Other Prevention Measures:

- Vaccinia immunization is approximately 85% effective in preventing human monkeypox disease, and CDC recommends its use for exposed people up to 14 days after the exposure.

Other Comments

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

Suggested Reading:

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