Case Definition

Monkeypox (MPX)
(Notifiable)

October 2022

1. **Disease Information**

1.1 General Disease and Pathogen Information: Monkeypox (MPX) is an infectious zoonotic disease caused by the monkeypox virus (MPXV) which is known to affect several susceptible mammals including certain rat species, squirrels, rabbits, prairie dogs, new- and old-world monkeys and apes, and a variety of other species. Further research is needed to better define the mammalian host range. MPX is endemic to western and central Africa where two viral clades persist. In humans, viruses in Clade II tend to produce mild clinical signs while viruses in Clade I have increased virulence[1]. In endemic areas, monkeypox virus is thought to be maintained in nature through circulation in wild rodents (including squirrels and certain rat species), with occasional spill-over to non-human primates and humans.

MPXV can be transmitted through direct contact with an infected animal or contaminated materials including saliva, urine, feces, and meat. Direct human-to-human transmission has been documented through close physical contact as well as respiratory droplets. Although some animal species are known to be susceptible, each suspected animal case, particularly for species not previously demonstrated to be susceptible to infection, may need additional testing to determine the true infection status given the lack of information available for the current circulating virus.

1.2 Clinical Signs:

1.2.1 Non-human Primates: The primary clinical sign is a self-limited rash, initially presenting as small cutaneous papules that develop into pustules and crust over. Lesions appear with an erythemic, necrotic center surrounded by epidermal hyperplasia and often scar after healing. There is a large variation in the number of pox lesions between primates; however, the most common locations to observe lesions is on the face, limbs, palms, soles, and tails. Rash may be accompanied by fever, lymphadenopathy and, in severe cases, respiratory signs, ocular discharge, facial edema, and anorexia.

1.2.2 Rodents: Clinical signs include fever, anorexia, blepharoconjunctivitis, depression, respiratory signs, diarrhea, and cutaneous lesions. Rarely, oral ulcers and lymphadenopathy is observed as well. Some species of rodents display only nonspecific clinical signs such as lethargy, conjunctivitis, and unkempt coat, while others are asymptomatic. African rodents are believed to be reservoir hosts; however, specific species have not been identified.

[1] WHO now refer to the former Congo Basin (Central African) clade as Clade one (I) and the former West African clade as Clade two (II). Additionally, it was agreed that the Clade II consists of two subclades.

1.2.3 Other species: more research or observational reporting is needed to define clinical signs.

2. Laboratory Criteria

2.1 Agent Isolation and Identification: Collect vesicle fluid by syringe and needle or swab ruptured vesicles, also collect any available scabs from older vesicles. If no skin lesions are present and there are alternative reasons to test, such as direct exposure to a case or viremia is suspected, collection of whole of blood in a purple top (EDTA) vacutainer tube. Mucocutaneous secretion, oropharyngeal or rectal swabs may be warranted. Keep samples as cold as possible without freezing. Tests include histopathology or electron microscopy, real-time polymerase chain reaction (rtPCR), genetic sequencing, immunohistochemistry (IHC), and virus isolation (VI).

2.2 Agent Characterization: Genome sequencing is available to differentiate viral clades and support genomic epidemiology.

2.3 Serology: Serological tests including virus neutralization and ELISA are available for detecting antibodies to orthopoxviruses. Currently, there are no assays specific to detecting MPXV antibodies; as such, the available diagnostic and epidemiologic information should be used when interpreting results.

3. Case Definition[2] and Reporting Criteria

3.1 Suspect Case:

3.1.1 an animal having clinical signs consistent with MPX; **AND**

3.1.2 an epidemiologic link to a confirmed human or animal MPX case, or other exposure of public and animal health concern.

3.2 Presumptive Positive Case: an animal with a non-negative screening laboratory test result for MPX (Histopathology, electron microscopy, IHC, Ab ELISA, rtPCR)

3.3 Confirmed Positive Case[3;4]:

3.3.1 an animal from which MPXV has been isolated; **OR**

3.3.2 identification of MPXV by rtPCR[5] **AND** genomic sequencing.

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[2] Given the re-emerging nature of this disease laboratories should select test(s) appropriate for the sample type and interpret results in the context of all available information for each case.

[3] Confirmatory testing must be conducted at either the Centers for Disease Control and Prevention (CDC) Poxvirus laboratory or the National Veterinary Services Laboratories (NVSL), Ames Iowa laboratory.

[4] An animal may be excluded as a confirmed case if any of the following applies:

- An alternative diagnosis can explain the illness fully. Factors that may be considered when assigning alternate diagnoses include the strength of the epidemiologic evidence for disease-specific exposure, the specificity of the alternate diagnostic test, and the compatibility of the clinical presentation and course of illness for the alternative diagnosis.
- Test result(s) are poorly or not repeatable, and resampling is either not possible, or testing from resampling is negative.
- Surface contamination cannot be ruled out with available case information and test results.

[5] If sufficient specimen volume is not available genomic sequencing will be prioritized and may be considered confirmatory if sequence of sufficient quality is obtained.