

Mpox and Pregnancy: What Maternal-Fetal Medicine Subspecialists Need to Know

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The Society for Maternal-Fetal Medicine (SMFM); Naima T. Joseph, MD; Brenna Hughes, MD; Jeffrey Kuller, MD; and Judette Louis, MD, MPH

In support of the November 28, 2022, <u>recommendation by the World Health Organization</u> (WHO) and Health and Human Services (HHS), SMFM will adopt "mpox" as the term used to refer to monkeypox disease.

Introduction

Since May 2022, the Centers for Disease Control and Prevention has been tracking cases of mpox virus infection in 47 states, Washington, D.C., and Puerto Rico. More than 28,000 cases in 88 countries have been confirmed globally, with 27,875 cases occurring in countries that have not historically reported mpox. Although data are limited, pregnant or breastfeeding people may be at heightened risk for worsened disease severity and adverse perinatal outcomes associated with mpox infection. This document complements the rapidly evolving guidance from the Centers for Disease Control and Prevention, focusing on unique maternal, fetal, and perinatal clinical considerations.

What is mpox, and how is it transmitted?

The mpox virus is an orthopoxvirus that exhibits features similar to smallpox or variola virus. Mpox virus has two different strains, one of which, the *Congo basin*, is associated with more severe illness and case fatality. The World Health Organization reports that the dominant circulating strain is the West African clade, which has a case fatality ratio of 3% to 6%.

Human-to-human transmission occurs from (1) direct contact with an infected rash, scab, or body fluid; (2) respiratory secretions during prolonged or intimate physical contact; and (3) contact with contaminated items, such as clothing or bedding. A person with mpox infection is considered contagious from initial viral prodrome and development of rash until the lesions have fully healed and new skin has formed over the scabs. It is not clear whether asymptomatic spread

occurs, nor is it clear if transmission can also occur through vaginal or seminal fluids. Perinatal infection can occur through transplacental transmission or during close contact during and after birth.

Zoonotic (animal-to-human) transmission also occurs following direct contact with the blood, bodily fluids, or cutaneous or mucosal lesions of infected animals.

What is the clinical presentation of mpox virus?

Patients may present with fever, lymphadenopathy, malaise, headache, myalgia, and rash. A vesicular or pustular rash typically develops 1 to 4 days after initial symptoms and can persist for 2 to 4 weeks. A wide spectrum of lesions have been reported but most often they are firm, vesicular, well-circumscribed or confluent. Historically, the lesions begin centrally and progress outwards to hands, feet or face. However in the current outbreak, the lesions have begun on or near the oral, genital and anal region.

Data regarding risk factors for infection and disease progression in this outbreak are informed from a recent case series of 528 laboratory-confirmed infections diagnosed between April 27 and June 24, 2022, at 43 sites in 16 countries. Among the group, 13% required hospital admission for pain and symptom control, including severe pain, severe pharyngitis limiting oral intake, acute kidney injury, and myocarditis, and 5% of the total cohort received mpox-specific treatment. No deaths occurred.

What are the pregnancy implications of mpox virus infection?

It is unknown if pregnant people are more susceptible to mpox virus acquisition or if the disease is more severe during pregnancy. However, an increased risk of maternal mortality and morbidity has been documented with other poxvirus infections.

Mpox virus can be transmitted to the fetus during pregnancy or to the newborn by close contact during and after birth. A commentary examined 5 cases with documented perinatal outcomes reported in the literature. Among these 5 cases, 2 resulted in spontaneous abortion, 1 resulted in stillbirth, and 1 resulted in the preterm birth of a neonate with congenital mpox infection and subsequent neonatal death. Other individual contributing circumstances are not known. The frequency and risk factors for disease severity and adverse pregnancy outcomes are also unknown.

What is the evaluation for a person with suspected mpox infection?

For any patient with a rash or anogenital lesion, clinicians should collect a detailed travel and sexual history and perform a physical examination that includes an evaluation of lymph nodes and oral, genital, and rectal mucosa.

Clinicians should isolate their patient in a single-person room if available. Clinicians should consult their infection and control practice in their hospital system, their state health department (State Contacts), or CDC through the CDC Emergency Operations Center (770-488-7100) as soon as mpox is suspected to ensure proper testing and reporting. Two-step diagnostic testing includes obtaining multiple samples from different lesions and sending the sample for an initial

orthopoxvirus polymerase chain reaction test. If orthopoxvirus is confirmed, the specimens are sent for mpox virus-specific testing. Co-infections with mpox virus and sexually transmitted infections (STIs) have been reported; therefore, a broad testing approach for STIs should be considered.

Additionally, <u>clinicians should use appropriate infection prevention measures</u> when collecting specimens for mpox evaluation. These measures include the use of personal protective equipment such as eye protection, gown, gloves, and a particulate respirator approved by the National Institute for Occupational Safety and Health (NIOSH), e.g. N95.

What treatment can be offered during pregnancy and lactation?

<u>Pregnant, recently pregnant, and breastfeeding people should be prioritized for medical treatment if needed</u>. Most infected people will have a mild, self-limiting illness. However, <u>CDC guidance</u> indicates that patients who should be considered for treatment following infection include:

- 1. People with severe disease and one or more complications requiring hospitalization (ie, hemorrhagic disease, encephalitis, secondary bacterial skin infection, poor oral intake, severe pain)
- 2. People at high risk of severe disease, including pregnant or breastfeeding people, people with immunocompromise, people with a history of active exfoliative skin conditions and pediatric patients, particularly those younger than age 8.

There are no specific treatments for mpox virus infection. Two antivirals and vaccinia immune globulin are available from the Strategic National Stockpile under expanded access investigational new drug protocols held by the Centers for Disease Control and Prevention. The risks and benefits of treatment should be discussed with the patient using shared decision-making.

Most people with infection have a mild, self-limiting illness. Severe disease includes hemorrhagic disease, sepsis, encephalitis, or other conditions requiring hospitalization.

Persons with mpox infection should also be counseled to isolate for the duration of the illness. The decision to treat and monitor a pregnant person as an outpatient or inpatient should be individualized. As CDC recommends, if treatment is indicated, tecovirimat should be considered the first-line antiviral drug for pregnant, recently pregnant, and breastfeeding people (see Table).

Table. Drugs Used for Treatment of Mpox

Drug	Availability	Administration	Pregnancy data	Breastfeeding data
Tecovirimat (TPOXX, ST-246)	Limited to health department/CDC expanded access protocol	Weight-based Intravenous and oral	Pregnant patients not included in pharmacokinetic studies Adverse events not observed in animal reproduction studies	Breastfeeding patients not included in pharmacokinetic studies Not known if present in breastmilk
Cidofovir (Vistide)	Off-label Available for use in an outbreak setting	Intravenous Contraindicated in patients with CrCl ≤55mL/min, serum Cr > 1.5 mg/dL; use with or within 7 days of nephrotoxic agents	No human data Animal data suggest embryolethality and teratogenicity	No human data Breastfeeding not recommended during period of exposed lesions
Brincidofovir (CMX001, Tembexa)	Availability limited to Strategic National Stockpile distribution	Oral Weight-based Dose adjustment for hepatic impairment No contraindications in manufacturer labeling	Animal data suggest embryolethality and teratogenicity	No human data Breastfeeding not recommended during period of exposed lesions
Vaccinia intravenous immune globulin (VIGIV)	Limited to health department/CDC expanded access protocol	Intravenous	No human or animal data Immune globulins known to cross the placenta without severe adverse effects	No human or animal data Immune globulins known to cross the placenta without severe adverse effects

CDC, Centers for Disease Control and Prevention; Cr, creatinine; CrCl, creatine clearance

Vaccines against mpox and administration during pregnancy

Two vaccines directed against mpox are currently available. ACAM2000 is a replicating viral vaccine licensed for the prevention of smallpox. It is contraindicated in pregnant or breastfeeding people due to the risk of pregnancy loss, congenital defects, and vaccinia virus infection.

JYNNEOS is a live, nonreplicating viral vaccine licensed for the prevention of both smallpox and mpox disease. Available human data on JYNNEOS administered to pregnant people are insufficient to determine if there are any vaccine-associated pregnancy-specific benefits or risks. Animal studies have not shown evidence of harm, and the vaccine should not be withheld from pregnant individuals who otherwise would be eligible in the context of shared decision-making. The JYNNEOS vaccine requires two doses administered 28 days apart for maximum effectiveness. Currently, JYNNEOS is in limited supply and available to individuals through state health departments who meet the following criteria:

- Postexposure prophylaxis either within 4 days of a known exposure to mpox to reduce the likelihood of infection or between 4 and 14 days postexposure which may reduce the severity of symptoms
- Known contacts of mpox cases identified by public health via case investigation, contact tracing, and risk exposure assessments (may include sexual partners, household contacts, and healthcare workers)
- Presumed contacts who meet the following criteria:
 - Know that a sexual partner in the past 14 days was diagnosed with mpox; or
 - Had multiple sexual partners in the past 14 days in a jurisdiction with known mpox

Coadministration with other vaccines: JYNNEOS typically may be given at the same time as other vaccines. However, because of the observed risk for myocarditis after receipt of ACAM2000 vaccine and mRNA and Novavax COVID-19 vaccines and the unknown risk for myocarditis after JYNNEOS, some people might consider waiting 4 weeks after JYNNEOS or ACAM2000 before receiving a Moderna, Novavax, or Pfizer-BioNTech COVID-19 vaccine. If an orthopoxvirus vaccine is recommended for prophylaxis in the setting of an outbreak, orthopoxvirus vaccination should not be delayed because of recent receipt of a Moderna, Novavax, or Pfizer-BioNTech COVID-19 vaccine; no minimum interval between COVID-19 vaccination with these vaccines and orthopoxvirus vaccination is necessary (CDC Vaccination).

Antenatal fetal surveillance for patients with suspected or confirmed mpox virus

Currently, the data are insufficient to guide recommendations for antepartum fetal surveillance. It is unknown when or how often vertical transmission occurs during pregnancy, nor how infection during pregnancy contributes to stillbirth risk. Fetal surveillance during acute illness should be guided by maternal disease severity, gestational age, and comorbid conditions. Clinicians can consider a follow-up growth ultrasound once the illness has resolved and following completion of the isolation period.

When and how should delivery occur in patients with mpox?

The relationship between the timing of infection in pregnancy, risk for congenital infection, and transplacental vs. intrapartum transmission is unknown. It is unclear whether preterm or early term delivery protects against adverse neonatal outcomes, nor is it clear whether cesarean delivery mediates the risk of perinatal infection. There has been no clear evidence of transmission through vaginal fluids; however, these data are limited. Further, nothing is known regarding genital tract shedding.

Currently, in the absence of obstetric indications, SMFM does not recommend preterm or early term delivery. Decisions regarding the mode of delivery should be individualized. Cesarean delivery can be considered if lesions are present and cannot be covered in or near the vaginal, anal, or perineal regions to reduce the risk of neonatal contact during delivery. However, the guidance will continue to evolve as pregnancy-specific data emerge.

Can patients with mpox virus breastfeed?

Mother-Infant Contact

While the benefits of skin-to-skin contact and rooming-in on breastfeeding are well-known, given the risk of neonatal transmission of mpox virus with close contact and the potential for severe disease in newborns, direct contact between a patient in isolation for mpox and their newborn is not advised. See <u>CDC</u> for additional considerations for mother-infant contact.

Infant Feeding with Breast Milk

Breast milk is the best source of nutrition for most newborns, and it provides protection against many illnesses. However, given that the mpox virus is spread by close contact and neonatal mpox infection may be severe, breastfeeding should be delayed until criteria for discontinuing isolation have been met (i.e., all lesions have resolved, the scabs have fallen off, and a fresh layer of intact skin has formed). Breast pumping will allow patients to maintain supply during a breastfeeding pause. However, until there are data evaluating the risk of transmission through breastmilk, current recommendations are to discard breastmilk pumped until the person is considered no longer infectious.

See <u>CDC</u> and <u>AAP</u> for additional information on infant feeding with breastmilk.

Infection Control

<u>Infection control practices</u> for the care of patients who are pregnant with mpox infection are the same as those for patients who are not pregnant with mpox infection — including appropriate isolation of patients with mpox; training for healthcare personnel on maternity and newborn care units on correct adherence to <u>infection control practices and PPE</u> (gown, gloves, eye protection, and NIOSH-approved particulate respirator equipped with an N95 filter or higher) use and handling; and ensuring sufficient and appropriate PPE supplies are positioned at all points of care.

Further, visitors to pregnant or postpartum patients with mpox should be limited to those essential to the patient's care and wellbeing. The use of alternative mechanisms for patient and visitor interactions, such as video-call applications, should be encouraged for any additional support.

Visitors should have no direct contact with the patient.

Further resources:

CDC: https://www.cdc.gov/poxvirus/monkeypox/index.html

ACOG: https://www.acog.org/clinical-information/physician-faqs/obstetric-care-considerations-monkeypox

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