INFORMATION PAPER

DHA-IHD
21 July 2022

SUBJECT: Mpox Disease and Mpox Vaccine

1. Purpose. To describe mpox disease and the new mpox vaccine, JYNNEOS

2. Facts.

   a. Microbiology. Mpox virus causes the contagious disease Mpox in humans. Mpox virus is a poxvirus of the genus *Orthopoxvirus*. *Orthopoxviruses* are large, complex, brick- shaped, double-stranded DNA viruses that cause infections characterized by a rash. Poxviruses have highly specialized modes of replication and pathogenesis allowing them to replicate in the cytoplasm of infected cells. Because it does not replicate in the host cell's nucleus, the poxvirus has no access to the host cell's transcription and DNA replication apparatus, and therefore, has a large genome to support all of its nuclear-replication processes.

   b. Disease. Mpox, a zoonotic disease for which the animal reservoir is unknown and is endemic in several Central and West African countries. There are two clades (strains) of Mpox virus, West African, and Congo Basin, the latter causing more severe illness. The West African clade has, to date, has been responsible for all cases reported in countries outside of Africa. The case fatality rate of mpox associated with the West African clade is less than 1%. Patients with mpox typically experience a febrile prodrome 5–13 days after exposure (range = 4–17 days), which often includes lymphadenopathy, malaise, headache, and muscle aches. The prodrome is followed 1–4 days later by the onset of a characteristic deep-seated, papular, vesicular, or pustular skin lesions with centrifugal distribution; the lesions are well circumscribed and often umbilicate or become confluent, progressing over time to scabs. The rash can be disseminated. Some cases have begun atypically, with lesions in the genital and perianal region and without subjective fever or other prodromal symptoms. For this reason, cases might be confused with more commonly seen infections such as varicella zoster or sexually transmitted infections (STIs) (e.g., genital herpes or syphilis).

      A person is considered infectious from the onset of illness until all lesions have crusted over, those crusts have separated, and a fresh layer of healthy skin has formed under the crust. Human-to-human transmission of

the West African clade occurs principally by direct contact with infected body fluids or lesions, and less so via infectious fomites or through respiratory secretions that typically require close, sustained contact. Currently, there are no specific treatments approved for mpox infection, although antivirals used to treat smallpox such as tecovirimat (TPOXX), cidofovir (Vistide), and brincidofovir (Tembexa) may be beneficial in certain cases. Additional treatment options to include use of Vaccinia Immune Globulin Intravenous (Human) (VIGIV) can be found in the interim clinical guidance by CDC at: https://www.cdc.gov/poxvirus/mpox/clinicians/treatment.html.

c. Testing. MTF providers have three options for mpox testing, i.e., referral to: 1) a State Public Health LRN-participating laboratory; 2) a DoD LRN-participating laboratory currently processing requests for non- variola orthopoxvirus testing; or 3) a commercial laboratory such as Labcorp, which holds the DoD's contract for reference laboratory testing services and is therefore the preferred commercial laboratory option for DoD. MTF providers should contact the Chief of Pathology/Laboratory Manager of their supporting laboratory service to determine the most efficient and effective testing options for their individual needs. Details and guidelines to obtain specimen to confirm mpox infection may be found in the DHA/IHD's Guideline for Obtaining suspected Mpox Polymerase Chain Reaction (PCR) Assay.

d. Epidemiology. In 2022, the identification of West African mpox cases in many non-endemic countries and in cases without travel history to an endemic region suggests person-to-person community spread. In this outbreak, most people have become infected with mpox when they come into close physical (skin-to-skin) contact with an infected person. The majority of confirmed cases had close or intimate in-person contact with persons in a social network experiencing mpox activity, including MSM who meet partners through an online website, digital app, or social event (e.g., a bar or party). Spread can occur from touching skin lesions, bodily fluids, or clothing or linens that have been in contact with an infected person. Spread can also occur during prolonged, face-to-face contact. Mpox can spread from person to person through:
    - Sexual or intimate contact (including oral, anal, and vaginal sex)
    - Hugging, kissing, cuddling, and massage
    - Sharing a bed, towel, or clothes that have not been washed

    It is also possible to contract mpox through contact with a dead or

live wild animal or exotic pet that is an African endemic species, or use a product derived from such animals (e.g., game meat)
Mpox does not spread from person to person through:

- Walking by someone who is infected
- Casual conversation with someone who is infected.

The following measures can be taken by the public to prevent infection with mpox:

- isolate ill persons from uninfected persons;
- practice good hand hygiene
- use appropriate personal protective equipment to protect household members if ill or caring for ill persons at home (e.g., a surgical mask, long sleeves and pants, and disposable gloves);
- use an Environmental Protection Agency–registered disinfectant with an emerging viral pathogens claim that is found on EPA's List Q for disinfection of surfaces. https://www.epa.gov/pesticide-registration/disinfectants-emerging-viral-pathogens-evps-list-q
- Patients should also avoid contact with pets and other animals while infectious because some mammals might be susceptible to mpox.

Persons with symptoms of mpox, including unexplained lesions, should contact their health care provider for an evaluation and should avoid close contact with others, including intimate or sexual contact, until they are evaluated.

e. Vaccine. A new, non-replicating vaccinia virus vaccine, JYNNEOS, was approved for preventing of mpox disease by the FDA in September 2019. Both JYNNEOS and ACAM2000 are available for preventing mpox infection. Both vaccines contain an orthopoxvirus called vaccinia. ACAM2000 vaccine contains a live, replicating virus that causes a local infection at the vaccination site. JYNNEOS contains non-replicating vaccinia virus and is considered the safer choice for most people. Use of ACAM2000 to prevent mpox is generally only appropriate for healthy people with documentation of prior ACAM2000 receipt more than 3 years ago. [See DHA IHD Smallpox Vaccine Information Paper.] About 97% of vaccinated individuals are protected after formation of the vaccination site pustule with ACAM2000 or about 2 weeks after administration of two doses of JYNNEOS administered one month apart.

f. Vaccine Handling. Note; the JYNNEOS manufacturer has provided guidance on expanded duration of storage at refrigerated temperatures that is different than indicated in the package insert. This updated guidance can be found at https://aspr.hhs.gov/SNS/Documents/MVA-BN-Information-Ltr-Effective-14June2022.pdf.

- The vaccine comes in single dose vials.

- Keep frozen at -25°C to -15°C (-13°F to +5°F) until expiration date.
- DO NOT store on dry ice or below -50°C (-58°F).
- Store in the original package to protect from light.
- Do not re-freeze a vial once it has been thawed.
- Once thawed, the vaccine may be kept at +2°C to +8°C (+36°F to +46°F) for up to 8 weeks. Count 8 weeks from when the vial was first thawed and mark this “beyond use date” (BUD) on the vial label. If the product expiration date on the carton is earlier, write that on the vial instead.
- Prior to administration, allow vaccine to thaw.
- Swirl the vial gently before use for at least 30 seconds. Withdraw a dose of 0.5 mL into a sterile syringe for subcutaneous injection.

g. Precautions. JYNNEOS contains live, non-replicating, vaccinia virus. All vaccinees (whether primary or revaccinee) must be screened for contraindications prior to vaccination using the most current DoD routine/general vaccine-screening form. JYNNEOS contains minute amounts of Gentamicin. Persons allergic to Gentamicin or who experienced a severe allergic reaction following a previous dose of JYNNEOS or following exposure to any component of JYNNEOS may be at increased risk for severe allergic reactions after JYNNEOS. Appropriate medical treatment must be available to manage possible anaphylactic reactions following administration of JYNNEOS.

1. Immunocompromised persons, including those receiving immunosuppressive therapy, may have a diminished immune response to JYNNEOS.

2. Pregnancy. While animal studies assessing fetal risk associated with JYNNEOS were reassuring, human data on JYNNEOS administered to pregnant patients are, at this time, insufficient to assess vaccine-associated risks in pregnancy. If JYNNEOS is administered to a pregnant patient, this should be reported to the DoD Smallpox Vaccine in Pregnancy Registry. [See DHA IHD Information Paper on this topic.]

3. Breastfeeding. It is not known whether JYNNEOS is excreted in human milk. Data are not available to assess the effects of JYNNEOS in the breastfed infant or on milk production/excretion. Because JYNNEOS contains no replicating virus, it should not create risk of transmission to a breastfed infant. CDC considers breastfeeding a precaution, but not a contraindication, to JYNNEOS receipt.

h. Immunization. Screen all potential vaccine recipients for eligibility for vaccination using the standardized immunization screening form available from the DHA Immunization Healthcare Division. Provide all eligible vaccinees a Vaccine Information Statement before vaccination to help educate them about potential risks associated with the vaccine.

For primary (naïve) vaccinees, administer two doses (0.5 mL each) of JYNNEOS at least 4 weeks apart by subcutaneous injection, preferably into the upper arm (deltoid). If previously vaccinated (with Dryvax, ACAM2000, or the 2-dose JYNNEOS series) only 1 dose of JYNNEOS is required for protection.

JYNNEOS may continue to be administered as a booster so long as exposure risk continues. However, there are inadequate data to determine the appropriate timing of booster doses. But, if considered necessary, a single 0.5 ml dose should be administered subcutaneously as follows:

- Every 2 yrs for individuals at High Risk (persons working with more virulent orthopoxviruses (e.g., Variola virus or Mpox virus))
- Every 10 yrs for individuals with occupational risk that is not considered High Risk (persons working with less virulent orthopox-viruses (e.g., Vaccinia virus or Cowpox virus) or other occupational exposures).

Although JYNNEOS is a live-virus vaccine, it is non-replicating, and therefore the 28-day interval associated with injected sequential live-virus vaccines does not apply.

JYNNEOS may be given at the same time as other vaccines. However, out of an abundance of caution, the CDC suggests that people at increased risk of myocarditis, including adolescent or young adult males, might consider waiting 4 weeks after JYNNEOS vaccination before getting an mRNA COVID-19 vaccine.

i. Adverse Events. There are side effects and risks associated with the JYNNEOS vaccine. Most people experience mild reactions that include injection site pain, redness, swelling, and/or itching; myalgia, headache, fatigue, fever, lymph node swelling, and nausea. Others, more rarely, have experienced neuropathy, abdominal pain, skin rash, rapid heart rate, chest pain, or angioedema. About 1:200 (0.5%) experienced EKG changes or cardiac enzyme elevations, suggestive of the myocarditis seen after the ACAM2000 vaccine. Studies are planned to define the risk of myocarditis, if any, associated with JYNNEOS vaccine. All personnel should report to a healthcare provider immediately if they develop any symptoms of concern. The Immunization Healthcare Division staff is available 24 hours a day at

877-438-8222, Option 1, to answer questions from vaccinees or the healthcare team.

j. DoD Policy. (19JUL2022)
There are two available smallpox vaccines (ACAM2000 and JYNNEOS) which may be considered for mpox pre-exposure (PrEP) and post-exposure prophylaxis (PEP). JYNNEOS is the only vaccine that is FDA approved for mpox prevention. Guidelines for use of PrEP and PEP vaccination are updated here: https://www.cdc.gov/poxvirus/mpox/clinicians/vaccines/vaccine-considerations.html
However, Jynneos vaccine is in very short supply presently and therefore must be allocated judiciously. Currently the categories for JYNNEOS acquisition and administration within the DOD, in order, are:
- PEP: All with high-risk contact with confirmed mpox case IAW CDC Exposure Categories
- PrEP: All laboratory workers identified as involved directly in the lysing step of the sample preparation in the DOD LRN labs currently engaged in orthopoxvirus sample testing
- PrEP: Allocated on a limited, case-by-case basis for those with high-risk behavior or healthcare occupation in high-risk settings/ geographic areas as defined by the CDC. Pre-positioning of vaccines in such high-risk situations will be considered as vaccine supplies increase.
- PrEP: Allocated on a limited, case-by-case basis for deployable response teams only if in direct support of civilian vaccination events in high-risk locations as defined by the CDC.

k. Special Considerations.
- Patients with atopic dermatitis experienced more redness, swelling, chills, and headache after JYNNEOS than patients without atopic dermatitis. While atopic dermatitis history is not a contraindication to JYNNEOS vaccination, all patients should be advised to report any adverse reactions.
- The safety and effectiveness of JYNNEOS have not been established in individuals less than 18 years of age.

3. References.

a. Defense Health Agency, Medical Affairs. Clinical Guidance for Mpox Testing, Public Health Reporting and Treatment Memo. https://health.mil/Reference-Center/Policies/2022/08/29/Clinical-Guidance-for-Mpox-Public-Health-Emergency

b. Centers for Disease Control and Prevention. Mpox Outbreak - Nine States, May 2022. MMWR 2022;71;1-6

c. CDC Health Alert Network. Updated Case-finding Guidance: Mpox Outbreak - United States, 2022 https://emergency.cdc.gov/han/2022/han00468.asp

d. Centers for Disease Control and Prevention. Use of JYNNEOS (Smallpox and Mpox Vaccine, Live, Nonreplicating) for Preexposure Vaccination of Persons at Risk for Occupational Exposure to Orthopoxviruses: Recommendations of the Advisory Committee on Immunization Practices - United States, 2022. MMWR 202271(22);734-42

e. Greenberg RN, Hurley MY, Dinh DV, et al. A Multicenter, Open-Label, Controlled Phase II Study to Evaluate Safety and Immunogenicity of MVA Smallpox Vaccine (IMVAMUNE) in 18–40 Year Old Subjects with Diagnosed Atopic Dermatitis. PLoS One. 2015; 10(10): e0142802.

f. JYNNEOS Package Insert dated 9/2019. Bavarian Nordic A/S, Denmark

g. Multiple resources (e.g., product insert, Vaccine Information Statements) assembled by the Immunization Healthcare Division.

North Atlantic Region Vaccine Safety Hub
Approved: Chief, Immunization Healthcare Branch
877-438-8222 (DSN 761-4245), Option 1