Monkeypox Resources To Consider

This list captures recent information shared by AABB and provides operational considerations for donor centers.

Updated Aug 31, 2022
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Monkeypox Resources and Information:

1) AABB’s Interim Monkeypox Fact Sheet and Monkeypox Summary
   A subgroup of the AABB Transfusion Transmitted Diseases (TTD) Committee recently updated the following information, which is available on the Emerging Infectious Diseases page of our website:
   - Interim Monkeypox Virus Fact Sheet updated July 27, 2022
   - Monkeypox Virus Summary updated August 31, 2022
   Provides considerations for:
     - Consignee Notification (Summary, page 4)
     - Donor Center Staff (Summary, page 6)
     - Disinfection (Summary, page 6)

   The TTD Committee continues to monitor the outbreak and will update this list as new information emerges.

2) FDA’s Information for Blood Establishments Regarding the Monkeypox Virus and Blood Donation
   - On Aug 12, 2022, FDA issued a Safety and Availability communication reiterating that existing safeguards provide sufficient protection against the potential for transfusion-transmission of monkeypox and ensure the continued safety and security of the blood supply.
   
   “Given the robustness of the existing safeguards for blood safety FDA does not recommend that blood establishments ask donors additional, specific questions about possible exposure to monkeypox virus,” the agency stated. “Further, FDA does not recommend using laboratory diagnostic tests to screen blood donors for monkeypox virus.”

3) Transfusion Transmission
   - There have been no documented cases of transfusion-transmitted Monkeypox. [Fact Sheet, page 3].

4) Blood Donor Considerations
   - No specific donor screening question is indicated at this time in the United States (US) as transfusion transmission has not been demonstrated. [Fact Sheet, page 5]
   - No FDA Guidance or AABB Standard has been issued at this time. [Fact Sheet, page 5]
   - The need for specific interventions to minimize a theoretical risk of transfusion transmission of Monkeypox Virus (MPV) 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.
     - 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. [Fact Sheet, page 2]

- 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 deferral interval is believed to be well beyond the duration of a putative MPV infectious viremia and high adherence to this donor criterion effectively mitigates any risk where donors continue to be directly questioned about MSM activity. [Fact Sheet, page 5]

- Optional Development of a Local Deferral:
  - A medical director always has the option to add additional, more restrictive questions to the Donor History Questionnaire v2.1 (DHQ), as described in the DHQ v2.1 User Brochure, page 5:
    - **Adding Questions:** Blood centers may choose to add “local” questions in the area designated for additional questions found at the end of the DHQ.
    - **This flexibility is built into the process, recognizing the medical director may elect to add additional donor screening criteria.**
    - The Fact Sheet, page 5, provides the following information for use by donor centers considering a local deferral:
      - 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.

5) Donor Eligibility Following Receipt of Vaccinations

- [FDA’s Key Facts About Monkeypox Vaccine](#) – Issued 07/29/22
- [Weekly Report article May 27, 2022](#):

  “REGULATORY UPDATE: TTD COMMITTEE RELEASES MONKEYPOX VIRUS OUTBREAK SUMMARY
May 27, 2022
AABB’s Transfusion Transmitted Diseases (TTD) Committee continues to monitor developments related to the ongoing outbreak of monkeypox. The Committee has prepared a monkeypox virus outbreak summary to inform members and provide current information about the outbreak. The summary contains up-to-date background information and donor considerations, including that the Food and Drug Administration recommends no donor deferral for pre-exposure receipt of the Jynneos vaccine for smallpox and monkeypox, provided the donor is otherwise healthy as required under 21 CFR 630.10 and section 630.15.

AABB reminds members that monkeypox is not known to be transfusion-transmissible and there have been no reports of transfusion-transmitted cases. Contact regulatory@aabb.org with questions."
DHQ v2.1 Flowchart, Question 8: [Summary, page 5]

**Question:** 8. In the past 8 weeks, have you had any vaccinations or other shots?

**Donor Eligibility:** Certain vaccinations may contain live infectious agents. A person who has been exposed to a live infectious agent in a vaccination should not donate for a specified period of time.

**Note on 8alt flowchart:** Some blood centers may choose to use a simpler but stricter deferral scheme in which all donors who received the smallpox vaccination are deferred for a minimum of 56 days, regardless of when the scab fell off. Blood centers using these criteria should use alternative Flowchart 8alt.

The Question 8 Flowchart has been modified to insert the following:
- **Green font** designates the pathway for the Jynneos vaccine
- **Red font** designates the pathway for the ACAM2000 vaccinia vaccine

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**Pathway for the ACAM2000 vaccinia vaccine**

- In the past 8 weeks, have you had any vaccinations or other shots?
  - Yes
    - Was the vaccination for smallpox?
      - Yes
        - When were you vaccinated for smallpox?
          - More than 21 days ago?
            - Yes
              - Defer donor until 21 days after the vaccination date.
            - No
              - Defer donor 56 days after vaccination date.
          - Fewer than 21 days ago?
            - Yes (continued)
            - No
              - Defer donor 56 days after vaccination date.
  - No
    - Accept donor

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**Pathway for Jynneos Vaccine**

- In the past 8 weeks, have you had any vaccinations or other shots?
  - Yes
    - Was the vaccination for smallpox?
      - Yes
        - When were you vaccinated for smallpox?
          - More than 21 days ago?
            - Yes
              - Defer donor for 21 days after vaccination date or until scab spontaneously falls off, whichever is later.
            - No
              - Defer donor until 21 days after the vaccination date.
          - Fewer than 21 days ago?
            - Yes (continued)
            - No
              - Defer donor 56 days after vaccination date.
  - No
    - Accept donor

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**NEXT PAGE:**

- Is the scab still on?
  - Yes
    - Defer donor for 21 days after vaccination date or until scab spontaneously falls off, whichever is later.
  - No
    - Did the scab(s) fall off by itself?
      - Yes
        - (continued)
      - No
        - Defer donor 56 days after vaccination date.
• AABB Standards for Blood Banks and Transfusion Services 33rd edition
Reference Standard 5.4.1A Requirements for Allogeneic Donor Qualification

<table>
<thead>
<tr>
<th>Category</th>
<th>Criteria/Description/Examples</th>
<th>Deferral Period</th>
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<tbody>
<tr>
<td>Immunizations and Vaccinations</td>
<td>• Receipt of Jynneos vaccine for Smallpox and Monkeypox (Attenuated, live, nonreplicating vaccine).</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td>• Smallpox Vaccinia Vaccine (Live virus vaccine comprised of Vaccinia Virus – “replication competent” vaccine)</td>
<td>Evaluate for deferral, as required in FDA Guidance²</td>
</tr>
</tbody>
</table>

6) FDA - Additional Information:

- FDA’s Information for Blood Establishments Regarding the Monkeypox Virus and Blood Donation

- FDA’s Update on Agency Response to Monkeypox Outbreak – July 29, 2022
In this bulletin FDA provides “an update to it’s multipronged response to monkeypox in the United States including its efforts in areas of diagnostics, vaccines and therapeutics.”

FDA Commissioner Robert M. Califf, M.D. stated “We understand that while we are still living with COVID-19, an emerging disease may leave people feeling concerned and uncertain, but it’s important to note that we already have medical products in place, specifically an FDA-approved vaccine for the prevention of monkeypox disease and an FDA-cleared diagnostic test. The FDA is using the full breadth of its authorities to make additional diagnostics and treatments available. We will continue to collaborate with our partners across all sectors to expand accessibility to countermeasures and bolster the tools in our arsenal as appropriate.”
- **FDA Monkeypox Response** – webpage describing FDA’s roles in monkeypox preparedness and response.

7) **Information shared by Dr. Lou Katz to AABB’s Transfusion Transmitted Diseases Committee meeting** - 08/03/22:

   **Slides begin on page 8**

8) **Human Cell, Tissue, and Cellular and Tissue-based Product (HCT/P) Considerations**

   - FDA’s [Important Information for Human Cell, Tissue, and Cellular and Tissue-based Product (HCT/P) Establishments Regarding Monkeypox Virus and HCT/P Donation](#)

   - Refer to AABB’s [Monkeypox Summary](#), Section 7 for additional information.
Monkeypox® US

Louie Katz MD
ImpactLife Blood Services
AABB TTD
8 August 2022

Major increase in human monkeypox incidence 30 years after smallpox vaccination campaigns cease in the Democratic Republic of Congo

“At the end of the smallpox eradication campaign, the Global Commission for the Certification of Smallpox Eradication concluded that continued smallpox vaccination to prevent monkeypox was not justified, despite the cross-protective immunity vaccinia vaccination provided against human monkeypox infection.”

Smallpox vaccination was officially discontinued in DRC in 1980.

Rimoin A et al. PNAS. 2010
“Classic” human monkeypox

- 1950s in non-human primates (lab outbreaks in Denmark)
- 1970 human infection. Now thousands of cases/year in endemic areas
- Animal reservoirs, so eradication unlikely c.f. smallpox
- US: 2003 outbreak (34 confirmed cases) from imported African rodents to prairie dogs in pet stores to humans. 2 travel-associated cases in 2021.
- 2 clades: Central & West African. Latter more clinically “mild”
- Animal-to-human: bites & scratches, body fluid contact & indirect from contaminated environment, bushmeat consumption
- Human-to-human: direct contact, droplets (rare), indirect from contaminated environment. STI?
- High clinical penetrance (conventional wisdom), asymptomatic not studied

Monkeypox

- Febrile prodrome (~2 days)
  - Less common in 2022 epidemic
- Macule to papule to vesicle to umbilicated vesicle to crust & detachment
- Mucosal involvement occurs
- Mortality 1-10% (depending on clade & availability of care)
  - 2022 outbreak mortality much lower than this
- Pediatric & immunocompromised hosts especially at risk for badness
  - Pneumonia
  - Encephalitis
  - Keratitis
  - Secondary bacterial infection
- Multiple mutations in 2022 strain of undetermined significance
Cumulative cases: Global & US: 7 Aug 2022

Monopox: Cumulative confirmed cases

https://ourworldindata.org/monkeypox

US 6598
Spain 4577
Germany 2887
UK 2759
France 2239
Brazil 1474
New York 1862
California 826
Florida 633
Texas 606
Illinois 602
Georgia 596

WHO, CDC

Characteristics of current infections: 3 Aug. 2022

- >99% male (at this point)
  - MSM predominate (>95%) among those for whom information on sexual behaviors is available
  - Esp. with multiple (median 5 in three months) & anonymous recent partners
  - High rates of HIV infection (=40%) & of PrEP use (57%)
  - Mean age 38 (range 18-68)
  - Mean incubation 7.6 days (95% CI: 6.2-9.7)
  - Worldwide mortality very low outside endemic countries, but substantial morbidity primarily related to pain

26,208 cases in 87 countries

344: 7 endemic countries
25,864: 80 non-endemic countries

Sources: CDC, WHO, Thornhill et al, NEJM. /2022
Current characteristics¹ (WHO, 3 Aug 2022), N=19326

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<tr>
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<th>Yes</th>
<th>No</th>
<th>Missing data</th>
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<tbody>
<tr>
<td>MSM</td>
<td>7328 (97.5%)</td>
<td>186 (2.5%)</td>
<td>11812</td>
</tr>
<tr>
<td>HIV-Positive</td>
<td>2979 (37.6%)</td>
<td>4944 (62.4%)</td>
<td>11403</td>
</tr>
<tr>
<td>Health worker</td>
<td>339 (13.5%)</td>
<td>2171 (86.5%)</td>
<td>16816</td>
</tr>
<tr>
<td>Travel History</td>
<td>785 (35.3%)</td>
<td>1438 (64.7%)</td>
<td>17103</td>
</tr>
<tr>
<td>Sexual Transmission</td>
<td>4807 (91.5%)</td>
<td>447 (8.5%)</td>
<td>14072</td>
</tr>
<tr>
<td>Hospitalized²</td>
<td>561 (7.1%)</td>
<td>7297 (92.9%)</td>
<td>11468</td>
</tr>
<tr>
<td>ICU</td>
<td>3 (0.1%)</td>
<td>3715 (99.9%)</td>
<td>15608</td>
</tr>
<tr>
<td>Died</td>
<td>2 (0.0%)</td>
<td>10652 (100.0%)</td>
<td>8672</td>
</tr>
</tbody>
</table>

¹ Includes endemic & epidemic countries
² May have been hospitalized for isolation or medical treatment

US Monkeypox

Epidemiologic and Clinical Characteristics of Monkeypox Cases — United States, May 17–July 22, 2022

Gender identity (1,196)

<table>
<thead>
<tr>
<th>No. (%)</th>
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<tbody>
<tr>
<td>Man (94% with recent MSM)</td>
</tr>
<tr>
<td>Transgender man</td>
</tr>
<tr>
<td>Woman</td>
</tr>
<tr>
<td>Transgender woman</td>
</tr>
<tr>
<td>Prefer not to answer</td>
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<tr>
<td>Missing</td>
</tr>
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</table>

Race & ethnicity (1,064)

<table>
<thead>
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<th>No. (%)</th>
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<tbody>
<tr>
<td>Asian, non-Hispanic</td>
</tr>
<tr>
<td>Black, non-Hispanic</td>
</tr>
<tr>
<td>White, non-Hispanic</td>
</tr>
<tr>
<td>Hispanic</td>
</tr>
<tr>
<td>Multiple, non-Hispanic</td>
</tr>
<tr>
<td>Missing</td>
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</table>

CDC.gov. 8 Aug. 2022

CDC. MMWR. 2022
Clinical to 22 July: US

<table>
<thead>
<tr>
<th>Sign/symptom</th>
<th>During illness* (N = 1,007)</th>
<th>At onset of illness (N = 461)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. (%)</td>
<td>No. (%)</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>Missing</td>
</tr>
<tr>
<td>Rash</td>
<td>1,004 (100.0)</td>
<td>0</td>
</tr>
<tr>
<td>Fever</td>
<td>596 (63.3)</td>
<td>345 (36.7)</td>
</tr>
<tr>
<td>Chills</td>
<td>550 (59.1)</td>
<td>381 (40.9)</td>
</tr>
<tr>
<td>Adenopathy</td>
<td>545 (58.5)</td>
<td>367 (41.5)</td>
</tr>
<tr>
<td>Malaise</td>
<td>531 (57.1)</td>
<td>399 (42.9)</td>
</tr>
<tr>
<td>Myalgia</td>
<td>507 (55.0)</td>
<td>415 (45.0)</td>
</tr>
<tr>
<td>Headache</td>
<td>469 (50.8)</td>
<td>454 (49.2)</td>
</tr>
<tr>
<td>Rectal pain</td>
<td>201 (21.9)</td>
<td>715 (78.1)</td>
</tr>
<tr>
<td>Pus/blood in stools</td>
<td>184 (20.5)</td>
<td>713 (79.5)</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>96 (11.5)</td>
<td>742 (88.5)</td>
</tr>
<tr>
<td>Rectal bleeding</td>
<td>90 (10.0)</td>
<td>810 (90.0)</td>
</tr>
<tr>
<td>Tenesmus</td>
<td>90 (10.0)</td>
<td>809 (90.0)</td>
</tr>
<tr>
<td>Nausea/vomiting</td>
<td>83 (9.2)</td>
<td>817 (90.8)</td>
</tr>
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</table>

*Percent calculated excluding missing data

Monkeypox prevention and control

- High-risk & exposed prophylaxis with (approved) “smallpox and monkeypox vaccine, live, non-replicating” (JYNNEOS) pre- & up to 14 days post-exposure. From MVA. Well tolerated
  - Receipt of the JYNNEOS for preexposure prevention requires no donor deferral
  - “Smallpox (vaccinia) vaccine, live” (ACAM-2000). Replication competent for use if above contraindicated? Associated with myo-pericarditis & many contraindications
- Hyperimmune globulin available for treatment
- Tecovirimat (TPOXX): approved for smallpox via “animal rule”. Protected NHP from fatal monkeypox virus infection
  - EUA for use during the current outbreak
  - RCT planned to start enrollment in Sept.
    - Off-label cidofovir or brincidofovir
- CDC for infection control/isolation/quarantine
  - [https://www.cdc.gov/poxvirus/monkeypox/clinicians/infection-control-home.html](https://www.cdc.gov/poxvirus/monkeypox/clinicians/infection-control-home.html)
Monkeypox and transfusion?

- No reported or alleged transfusion transmission
- “DNA-emia”, as viremia proxy, in a proportion of human infections
  - Little data on presence of infectious virus in humans (that available is negative)
  - Virtually no data on presymptomatic viremia/DNA-emia
- IV transmission & infectious viremia documented in NHP & other animal models
- 2003 outbreak in US (34 confirmed cases)
  - No mandated donor interventions
  - CBER: no recommendations except deferral for recent smallpox vaccination
    (which was/is recommended for monkeypox exposure)
- Donors must be well & the skin of the donation site must be inspected & intact
  - No validated donor history questions or education materials
  - No screening assays suitable for donors, but NAT companies are engaged

Nee S et al. Research Square. 2022. DOI: https://doi.org/10.21203/rs.3.rs-172583l/v1

EID fact sheet

- 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, & 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 & high adherence to this donor criterion effectively mitigates any risk where donors continue to be deferred for MSM activity*
  - In much of the world, the MSM deferral has been discarded & 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 & new sex partners & 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.

*Also for receipt of PrEP
Whither monkeypox—discussion points for TTD

- At this stage of the U.S. outbreak, are specific measures necessary to prevent phlebotomy of infected donors e.g., written materials, direct questioning, enhanced examination, donor testing?
  
  - For donors of SOHO the ECDC recommends that...
    
    “...potential donors should be carefully interviewed regarding contacts with infected (confirmed or suspected) MPX cases, infected animals or travels to affected areas....”
  
- (At least) 21-days deferral if donor volunteers contact with monkeypox?
- Deferral of infected until all lesions healed (reepithelialized)?
- Consignee notification of prior donations from infected &/or contacts and advice to hospitals on how to respond?

TTD to monitor the evolving epidemic & update membership PRN