Association for the Advancement of Blood & Biotherapies

Mpox
(formerly Monkeypox)
Resources To Consider

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

Updated Feb 26, 2024

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Monkeypox Resources and Information:

1) **AABB's Mpox Fact Sheet (formerly Monkeypox)**
   A subgroup of the AABB Transfusion Transmitted Diseases (TTD) Committee recently published a supplement to *Transfusion* containing new and updated Fact Sheets including the Mpox Fact Sheet, which is also available on the Emerging Infectious Diseases page of our website:
   - Mpox Virus Fact Sheet (formerly Monkeypox) - updated February 2024 *Transfusion*, page S142-S147.

   The TTD Committee continues to monitor the outbreak and will update the Fact Sheets 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 Mpox. [Fact Sheet, page S143].

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 S145]
   - No FDA Guidance or AABB Standard has been issued at this time. [Fact Sheet, page S145]
   - The need for specific interventions to minimize a theoretical risk of transfusion transmission of Mpox 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.
     - Since 2020 in the US, MSM have been specifically deferred for 3 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 MPV infectious viremia and high adherence to this donor criterion effectively mitigates any risk where donors continue to be directly

questioned about MSM activity.
    - The US policy was changed by the FDA in May 2023 with most blood collection organizations planning to implement the change to an individual donor assessment by summer-fall 2023. According to the new policy, any individual with a new sexual partner or multiple partners, either engaging in anal sex within the prior 3 months, will be deferred for 3 months.
    - In much of the world, the MSM deferral has been discarded and replaced by individual donor assessments. [Fact Sheet, page S145]
- Optional Development of a Local Deferral:
    - A medical director always has the option to add additional, more restrictive questions to the Donor History Questionnaire v4.0 (DHQ), as described in the DHQ v4.0 User Brochure, page 6:
        - **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 S145, 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 – Current as of 08/18/22

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.

DHQ v4.0 Flowchart, Question 9:

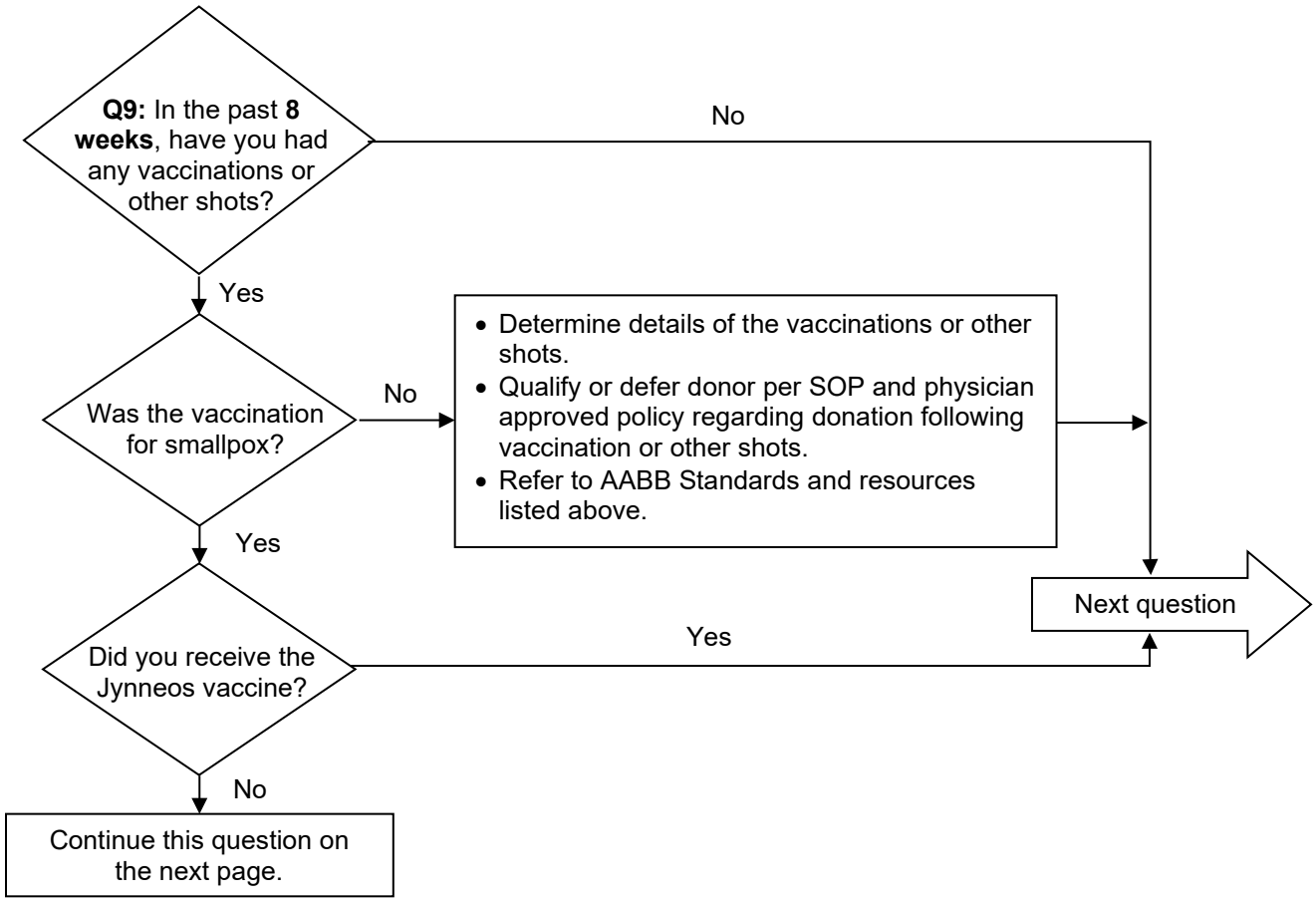
Question 9: In the past **8 weeks**, have you had any vaccinations or other shots?

Donor Eligibility: FDA recommends deferral for replication-competent smallpox vaccines as stated in FDA's December 2002 Guidance, *Recommendations for Deferral of Donors and Quarantine and Retrieval of Blood and Blood Products in Recent Recipients of Smallpox Vaccine (Vaccinia Virus) and Certain Contacts of Smallpox Vaccine Recipients Smallpox Vaccine* and consistent with the flowchart below. Donors are not automatically deferred following other vaccinations and the vaccine deferral policy is determined by the responsible physician. When developing a deferral policy, the physician may consider the following:

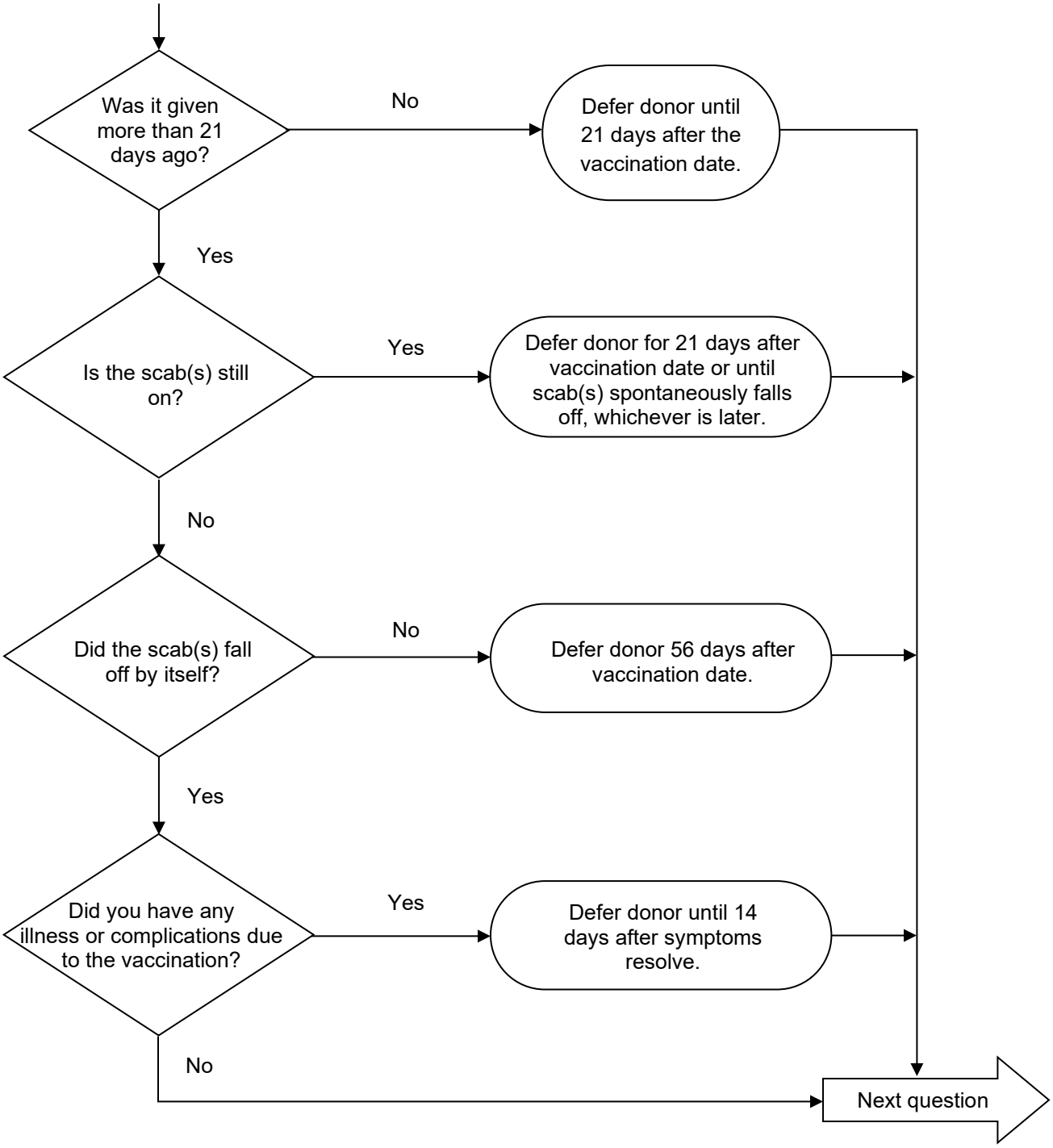
When developing a deferral policy and SOPs, the physician may consider the following:

- **AABB ACCREDITED FACILITIES:** Refer to the current edition of the Standards for Blood Banks and Transfusion Services Reference Standard 5.4.1A for immunization and vaccination deferral requirements and *AABB's Updated Information on Donation of CCP, Blood Components and HCT/Ps During the COVID-19 Pandemic*.

Note on 9alt Flowchart: The **9alt Flowchart** provides a simpler but more restrictive 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 **9alt Flowchart**.



Flowchart Question 9 continued:



- **AABB Standards for Blood Banks and Transfusion Services 33rd edition**

Reference Standard 5.4.1A Requirements for Allogeneic Donor Qualification

Category	Criteria/Description/Examples	Deferral Period
Immunizations and Vaccinations	• **Receipt of Jynneos vaccine** for Smallpox and **Monkeypox** (Attenuated, live, nonreplicating vaccine).	**None**
	• **Smallpox Vaccinia Vaccine** (Live virus vaccine comprised of Vaccinia Virus – "replication competent" vaccine)	**Evaluate for deferral, as required in** FDA Guidance[2]

6) Consignee Notification Considerations

If a blood collection organization receives information that a donor has received a diagnosis of MPV infection after donation and decides to notify consignees of this information and voluntarily withdraw untransfused in-date products, the most appropriate message is that the MPV has never been shown to be transmitted by transfusion, the donor was healthy at the time of donation and that the risk, if any, is believed to be minimal.

7) Donor Center Staff Considerations:

- Donor center staff reporting a Monkeypox infection:
  - The staff member should follow CDC guidance and remain isolated at home at least until signs and symptoms are gone, all scabs have separated, and the skin healed.
  - According to CDC, "a person with monkeypox can spread it to others from the time symptoms start until the rash has fully healed and a fresh layer of skin has formed. The illness typically lasts 2–4 weeks."
- Donor center staff reporting a Monkeypox exposure
  - Assess the nature of the exposure. Was it a close contact exposure? According to CDC, a close contact is:
    - Direct contact with monkeypox rash, scabs, or body fluids from a person with monkeypox.
    - Touching objects, fabrics (clothing, bedding, or towels), and surfaces that have been used by someone with monkeypox.
    - Contact with respiratory secretions.
  - Such employees should be monitored for the development of illness for 21 days. Isolation is recommended for those who develop an illness consistent with monkeypox.
- Notification of donor center staff following exposure in the donor center
  - Consider notification of donor center staff following an exposure to an individual with a confirmed Monkeypox infection to facilitate monitoring for illness.
- Notification of donors following an exposure in the donor center
  - Consider notification of donors following an exposure to an individual with a confirmed Monkeypox infection.

8) **Disinfection Considerations:**
   - Refer to CDC's Monkeypox>Healthcare Professionals>Infection Control

9) **FDA - Additional Information:**
   - FDA's Information for Blood Establishments Regarding the Monkeypox Virus and Blood Donation – current as of 08/12/2022

   - 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 – current as of 03/30/23

10) **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 – 08/29/22

    - Worldwide there have been no reports of transmission of monkeypox virus through use of human cells, tissues, or cellular or tissue-based products (HCT/Ps); therefore, the risk of infection transmitted by implantation, transplantation, infusion, or transfer of HCT/Ps remains theoretical.
    - Routine screening measures are already in place for evaluating risk factors and conditions as well as clinical evidence and physical evidence of infection in HCT/P donors. Allogeneic donor screening includes a donor medical history interview and review of relevant medical records to look for risk factors and conditions that may lead to a determination that a donor is ineligible. Accordingly, "due to the robustness of existing donor screening recommendations," the agency does not recommend using laboratory diagnostic tests to screen HCT/P donors for monkeypox virus.
    - Existing regulations require that the HCT/P establishment's responsible person must determine and document the eligibility of an allogeneic cell or tissue donor. Similar to their approach early in the COVID-19 pandemic, FDA stated that, based on information available at this time, establishments may wish to consider, whether, in the 21 days prior to HCT/P recovery, the donor:
      - was diagnosed with or was suspected of having a monkeypox infection;

  - had close contact with a person or an animal diagnosed with or suspected of having monkeypox infection regardless of the donor's vaccination status; or developed a rash or other symptoms suggestive of monkeypox infection.
- For donors who have received a vaccine:
  - the ACAM2000 vaccine, a licensed live replicating virus vaccine indicated for active immunization against smallpox that may be used against monkeypox, recommendations outlined in the 2007 guidance on HCT/P donor eligibility remain applicable. The guidance also includes recommendations for donors with clinically recognizable vaccinia virus infection from contact with someone who received a live replicating virus smallpox vaccine.
  - The licensed non-replicating virus vaccine indicated for prevention of monkeypox (JYNNEOS) does not carry this same concern.
- For cadaveric (non-heart-beating) donors, FDA recommended that HCT/P establishments determine whether an autopsy was not performed due to a perceived risk of transmission of communicable disease or, if an autopsy was performed, whether any special precautions were taken that would suggest there was a special concern over the risk of transmission of a communicable disease from the donor.

11) Information shared by Dr. Lou Katz to AABB's Transfusion Transmitted Diseases Committee meeting - 08/03/22

Slides begin on page 10

Monkeypox Я US

Louie Katz MD
ImpactLife Blood Services
AABB TTD
8 August 2022

1

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

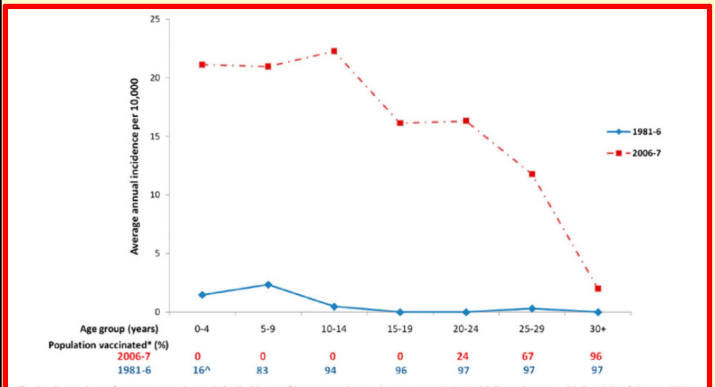


Fig. 4. Comparison of average annual cumulative incidence of human monkeypox by age group Kole Health Zone, Demographic Republic of Congo: 1981–86 vs. 2006–7. *, proportion of the population vaccinated in 2006–7 and in 1981–6 based on vaccination scar surveys in 1981–6 and in 2006. ^, vaccination rate steadily declined from 41.0% in 1981 to 4% in 1985 (13, 33).

"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

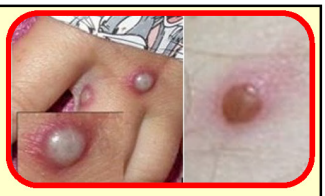
2

"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

3

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

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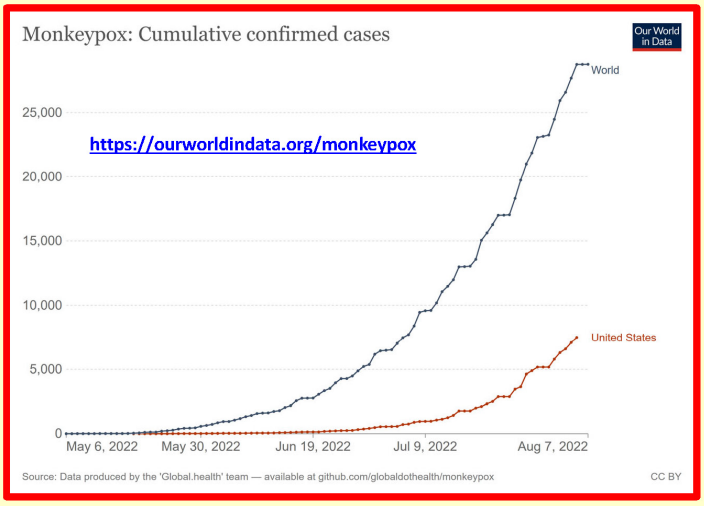
Cumulative cases: Global & US: 7 Aug 2022



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

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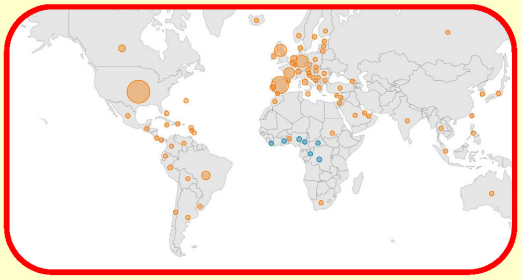
Characteristics of current infections: 3 Aug. 2022

- >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
25,684: 80 non-endemic countries



Sources: CDC, WHO, Thornhill *et al. NEJM. I2022*

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Current characteristics[1] (WHO, 3 Aug 2022), N=19326

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

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

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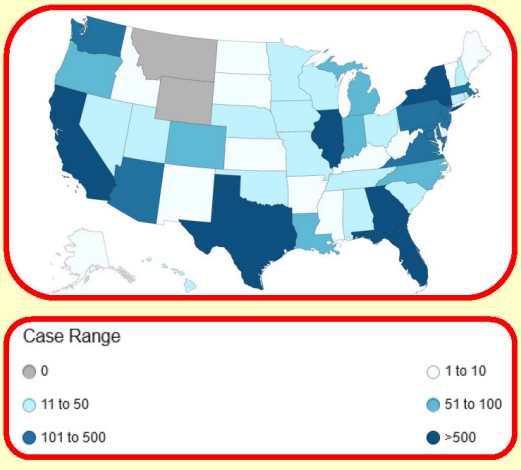
US Monkeypox



CDC.gov. 8 Aug. 2022

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

Gender identity (1,195)	No. (%)
Man (94% with recent MSM)	1,178 (98.7)
Transgender man	3 (0.3)
Woman	5 (0.4)
Transgender woman	5 (0.4)
Prefer not to answer	4 (0.3)
Missing	0 (0.0)
Race & ethnicity (1,054)	
Asian, non-Hispanic	48 (4.6)
Black, non-Hispanic	276 (26.2)
White, non-Hispanic	428 (40.6)
Hispanic	296 (28.1)
Multiple, non-Hispanic	6 (0.6)
Missing	141

CDC. *MMWR*. 2022

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Clinical to 22 July: US

Sign/symptom	During illness* (N = 1,007) No. (%) Yes	No	Missing	At onset of illness (N = 461) No. (%) Yes	No	Missing
Rash	1,004 (100.0)	0	3	121 (41.6)	170 (58.4)	170
Fever	596 (63.3)	345 (36.7)	66	120 (41.2)	171 (58.8)	170
Chills	550 (59.1)	381 (40.9)	76	48 (16.5)	243 (83.5)	170
Adenopathy	545 (58.5)	387 (41.5)	75	23 (7.9)	268 (92.1)	170
Malaise	531 (57.1)	399 (42.9)	77	24 (8.2)	267 (91.8)	170
Myalgia	507 (55.0)	415 (45.0)	85	13 (4.5)	278 (95.5)	170
Headache	469 (50.8)	454 (49.2)	84	27 (9.3)	264 (90.7)	170
Rectal pain	201 (21.9)	715 (78.1)	91	0 (0.0)	291 (100)	170
Pus/blood in stools	184 (20.5)	713 (79.5)	110	0 (0.0)	291 (100)	170
Abdominal pain	96 (11.5)	742 (88.5)	169	1 (0.3)	290 (99.7)	170
Rectal bleeding	90 (10.0)	810 (90.0)	107	0 (0.0)	291 (100)	170
Tenesmus	90 (10.0)	809 (90.0)	108	2 (0.7)	289 (99.3)	170
Nausea/vomiting	83 (9.2)	817 (90.8)	107	0 (0.0)	291 (100)	170

*Percents calculated excluding missing data

CDC. *MMWR. 2022*

9

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**

10

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

Parker S and Butler RM. *Future Virol.* 2013.
Adler H et al. *Lancet ID.* 2022.
Johnson RF *et al. J. Virol.* 2011.
Noe S *et al. Research Square.* 2022. DOI: https://doi.org/10.21203/rs.3.rs-1725831/v1

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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

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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

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