

CDC/IDSA Clinician Call
Clinical Management and Prevention of Clade II Mpox:
Plus, HPAI Update
- Jointly hosted with HIVMA
June 5, 2024

Q&A

This is the Q&A transcript from the Zoom webinar held on June 5, 2024. The views and opinions expressed here are those of the presenters and do not necessarily reflect the official policy or position of the CDC or IDSA. Involvement of CDC and IDSA should not be viewed as endorsement of any entity or individual involved.

- 1. Why does simple conjunctivitis come to the attention of CDC when in clinical practice symptomatic care is recommended and spontaneous resolution is expected. Often an antibacterial is prescribed even though viral etiology is expected. Please clarify so clinicians don't think antivirals should be used for simple conjunctivitis. Are we supposed to treat conjunctivitis without respiratory symptoms with antivirals?**

Jay Butler, MD FIDSA: The setting of the case, i.e., in the first 2 weeks after H5N1 was identified in the dairy herd to which the individual was exposed, increased the clinical suspicion, and led to testing. Of note, other avian influenza strains have occasionally caused conjunctivitis in the past.

- 2. Will commercial influenza diagnostic tests identify patients as positive for this influenza A?**

Jay Butler, MD FIDSA: Qualified yes--many of the commercial tests evaluated to date by FDA appear to detect H5N1, although they do not distinguish among hemagglutinin types. The qualification is that some antigen tests appear to have lower sensitivity.

- 3. How long should patients with H5N1 be isolated?**

Jay Butler, MD FIDSA: The guideline for novel influenza viruses would apply (which is different from the seasonal flu guideline and is a bit more vague because of the potential for different strains to behave differently).

- 4. Did USDA lab Ames Iowa identify cases in cows and cats or were these H5N1 studies done at the CDC?**

Jay Butler, MD FIDSA: Animal specimens are tested by USDA with subsequent sharing of specimens and sequences.

- 5. Why is it that when chickens are infected with avian flu, the herds are culled but there has been no culling of cows.**

Jay Butler, MD FIDSA: The key is in the name High Path AI. The mortality rate among the chickens is very high--culling is a measure to prevent spread from the small number of survivors. The illness in cows is quite mild, based on the experience to date.

- 6. Standard Influenza rapid tests do not detect H5N1, what new tests are under development or approved for H5N1? Are the primers available for PCR commercial lab detection for H5N1?**

Jay Butler, MD FIDSA: Test evaluated by FDA appear to detect H5N1, but there is concern that sensitivity may be reduced. If suspicion is high, would use PCR. Commercial lab capacity is scaling up in concert with public health labs.

- 7. What is the recovery of influenza in dairy herds? Is harvested milk continued during illness and is it safe on herd recovery? Or does Pasteurization make this milk issue a moot point?**

Jay Butler, MD FIDSA: Important question! The cows generally recover clinical in <10 days. The duration to viral shedding is a hot topic in the field work being conducted by USDA. You are correct that pasteurization makes the mild non-infectious, but the high viral load in milk raises concern about the role of milk in transmission in the barns.

- 8. Is there any plan to vaccinate farmers with the stockpiled vaccines?**

Jay Butler, MD FIDSA: At this time, it is being discussed as a potential strategy.

- 9. Is there an effort to reach out to eye Physicians?**

Jay Butler, MD FIDSA: Yes

- 10. Can you address the issue of the feeding of cattle using chicken waste as a way in which our bovines became infected? Shouldn't we also discuss that beef should not be eaten raw?**

Jay Butler, MD FIDSA: The mode of transmission among cattle has not yet been determined, but I agree with you that contamination of feeds (as is thought to occur among cats in Poland in the past) is one possibility.

- 11. To your knowledge, have any cases of H5N1 influenza been identified in backyard flocks? Do you have any advice for families who keep chickens not on farms, but in an urban setting?**

Jay Butler, MD FIDSA: Yes, H5N1 has been identified in hundreds of back yard flocks throughout North America. CDC and USDA have specific recommendations for backyard flocks on their websites.

- 12. When will we know about testing of raw milk and any reported illnesses from raw milk. I understand that the advisory to avoid raw milk were ignored and a rumor spread that drinking raw milk would protect the drinker.**

Jay Butler, MD FIDSA: Good example of very dangerous health misinformation! Mice have been infected with unpasteurized milk in lab settings. To date, no humans have had infection confirmed as being due to drinking unpasteurized milk. However, the risk seems very real--another reason to not drink raw milk.

- 13. Do you have any Ct data for H5N1 results from the May 30th case? If so, did the values trend with the Texas case from April 1st (low Ct for conjunctival, high Ct for respiratory)?**

Jay Butler, MD FIDSA: The Ct values in the 2nd MI case were quite high, so it is too early to say--but I share your interest in this observation!

- 14. Has the route of human infection in these cases been determined? What is known about the risk of infection after ingestion of H5N1 contaminated unpasteurized milk?**

Jay Butler, MD FIDSA: The route of cow to human transmission has not been confirmed. The mouse feeding studies using raw milk raise serious concerns about the risk of infection from drinking raw milk.

- 15. There seems to be a lot of pushback from the cattle farmers about addressing the H5N1 threat. How will this be handled?**

Jay Butler, MD FIDSA: Yes, there are a number of reasons why the workers would not want to trust government investigators.

- 16. Sanofi Pasteur's H5N1 Inactivated monovalent vaccine (licensed in 2007) is for clade 0 not for clade 2 (let alone the clade 2.3.4.4b that is currently circulating). The same is true for GlaxoSmithKline's Prepandrix. But what can you tell us about CSL Seqirus's AUDENZ and the Recombinant Protein Vaccines, Virus-Like Particle vaccines, Cell-Based Vaccines, DNA Vaccines, Live Attenuated Influenza Vaccines, and mRNA vaccines (e.g. U of Pennsylvania's Perelman School of Medicine, Moderna, and Pfizer are all developing an mRNA vaccine for the clade 2.3.4.4b H5 isolate)? Which can we expect to be ready by this fall?**

Jay Butler, MD FIDSA: The CVVs that we currently have are from much more recent isolates and have been utilized to produce the limited supply of vaccine that we currently have. Timeline for mRNA vaccines will depend on the success of the current trials.

17. FYI WHO confirms first fatal human case of bird flu A(H5N2).

<https://www.reuters.com/world/americas/who-confirms-first-human-case-avian-influenza-ah5n2-mexico-2024-06-05/> Please notice the news says, H5N2, not H5N1, but preliminary data indicates the H5 is of the 2.3.4.4b clade. We need to be alert for other H5Nx versions of influenza A, there is also a serious study from China of an H5N8 that is highly pathogenic for mammals (and is also an H of the 2.3.4.4b clade). Please address these concerns.

Jay Butler, MD FIDSA: Agree! H7 and H9 are also of concern.

18. Dr Butler, do we know the molecular drivers of HPAI transmission and virulence, and what are the priorities for HPAI genomic surveillance moving forward?

Jay Butler, MD FIDSA: Priorities going forward are to obtain specimens from a variety of infected birds and mammals in order to assess genetic changes that may be driving transmission. USDA's genetic assessment suggests that the jump from birds to cattle occurred 4-5 months before the first case was identified.

19. Do you know if the full sequences have been shared? That will help understand if these are re-assortments and allow the smart evolutionary biologists to estimate when the gene segments came together in the H5N2. H5N8 has been a concern for a while. Here is a 2021 reference <https://www.science.org/doi/10.1126/science.abg6302>

Jay Butler, MD FIDSA: Yes--I believe that the full sequence from the TX human case is included in the supplementary materials in the NEJM report. Best quick overview is at [https://www.who.int/publications/m/item/genetic-and-antigenic-characteristics-of-clade-2.3.4.4b-a\(h5n1\)-viruses-identified-in-dairy-cattle-in-the-united-states-of-america](https://www.who.int/publications/m/item/genetic-and-antigenic-characteristics-of-clade-2.3.4.4b-a(h5n1)-viruses-identified-in-dairy-cattle-in-the-united-states-of-america)

20. Will the case-by-case evaluation be deferred to local DoH or will be done only by the CDC? If that is the case please provide the contact information.

Jay Butler, MD FIDSA: CDC does not have the legal authority to do the case evaluations apart from the invitation from the state or local agencies.

21. Do we know how long H5N1 infections have been present in cows?

Jay Butler, MD FIDSA: USDA has issued a pre-print indicating that the jump to cattle from birds in Texas occurred about 4 months before the first herd infection was identified.

22. Are mRNA platforms being relied upon to expand existing H5N1 vaccine? what plans do the vaccine manufacturers have to rapidly expand availability?

Jay Butler, MD FIDSA: mRNA platforms are an exciting addition to the H5N1 prevention tools, in addition to egg- and cell-based vaccines.

23. Efficacy of ultra-high temp. flash Pasteurization that is currently used for processing commercial dairy products- where can we see real-world data on its efficacy for the current H5N1 clade of concern?

Jay Butler, MD FIDSA: FDA is doing those studies; I do not know if a detailed report has been issued yet. Research in Canada and EU with spiked milk specimens is encouraging that pasteurization should be successful.

24. For severely immune suppressed patients (I have a few HIV+ patients who have SOT's), they received their initial 2 doses 2 years ago. Should they get an additional dose, if they have an "active" social life?

Agam Rao, MD, FIDSA: At this time, we aren't recommending additional vaccine doses, including for severely immunocompromised patients. As I mentioned, additional vaccine doses doesn't come with negatives: increased reactogenicity could occur as we've observed in DRC. That aside, in a severely immunocompromised patient, it's unclear how effective the vaccine would be so the counseling I mentioned would be critical for this patient.

25. Should sites who are in the TPOXX EA IND program plan to keep their IRB continuously open?

Patty Yu, MPH: Sites can continue to keep their IRB protocols open for potential treatment of patients under CDC-sponsored EA-IND who meet eligibility protocol. Protocol-related updates will be posted on <https://www.cdc.gov/poxvirus/mpox/clinicians/obtaining-tecovirimat.html>. An updated letter from CDC IRB approving continuation of the protocol will be posted before the protocol's July 23, 2024 expiry.

26. Have there been any vaccine-associated cases in severely immune compromised patients?

Boghuma Titanji, MD, MSc, DTM&H, PhD: Jynneos is based on modified vaccinia Ankara virus which has very limited replication and there are currently no cases of vaccine associated infection in immunocompromised people. It is considered a safe vaccine in this group. Older generation vaccines which are replication competent like ACAM2000 are contraindicated.

Agam Rao, MD, FIDSA: Agree with Boghuma. It's a nonreplicating virus vaccine so the "live" part is misleading. It is actually a vaccine recommended to be given to immunocompromised patients unlike ACAM2000, the other orthopoxvirus in the United States (which is a live, replicating virus vaccine). JYNNEOS was even studied in immunocompromised patients.

27. Are there cohorts following persons with 2 doses to assess long term VE similar to the VE studies of Hep B vax done in AK?

Agam Rao, MD, FIDSA: Is this for mpox? If so, there is a smallish study by UCLA that might do this. We have a multijurisdictional study that might help us and also the DRC study that I mentioned. We also are evaluating infections after 2 doses of JYNNEOS (as I mentioned during the presentation) to see if there is a trend. Others should absolutely do their own evaluations; however, it's not clear that antibody levels alone is an indication of protection so that is one caveat to interpreting data.

28. I recently became aware of persons having 3 Jynneos Mpox vaccines. Under what circumstances would a person receive 3 doses?

Agam Rao, MD, FIDSA: The only people who, at this time, should be receiving more than 2 JYNNEOS doses are certain laboratorians at risk for exposure to MPXV or Variola virus because of their laboratory work. This MMWR describes those laboratorians. They are not your typical clinical laboratorians. Please feel free to reach out to poxvirus@cdc.gov if you have any questions about that.

https://www.cdc.gov/mmwr/volumes/71/wr/mm7122e1.htm?s_cid=mm7122e1_w

29. Where do you envision people getting the Jynneos?

Meghan Pennini, PhD: They should be able to access Jynneos as they do other routine vaccinations.

30. Can there be an exchange of genetic material between MPox Clade 1 and Clade 2? Is this possible?

Boghuma Titanji, MD, MSc, DTM&H, PhD: This is possible if both viruses are co-circulating as orthopoxviruses are well described to be capable of recombining their genomes. This is well reported in the literature with other poxviruses so is possible.

31. What are the surveillance strategies for Clade 1 in the US?

Agam Rao, MD, FIDSA: all MPXV isolates are being evaluated by Clade specific testing, including those tested at commercial laboratories. We have developed interim guidance which I presented during the March CDC-IDSA clinician call that I believe was recorded.

Some additional information about what we are doing in DRC is in this short article:

https://www.cdc.gov/mmwr/volumes/73/wr/mm7319a3.htm?s_cid=mm7319a3_w

32. MPOXV Clade 1 in the DRC outbreak seems to be causing a lot of household transmission, including children, as well as newly recognized (or at least acknowledged) transmission among MSM. Do we have more up to date epidemiologic data, and what might we anticipate if we have Clade 1 introduction?

Boghuma Titanji, MD, MSc, DTM&H, PhD: You are correct that transmission of clade 1 through sexual networks of MSM and CSW in DRC has recently been described and seems to be playing an important role in the ongoing outbreaks there. This means that if introduced to the US we could see it spread in a similar fashion as we saw clade II spread. historically and in current outbreaks in DRC children have been disproportionately infected and this may be due to the fact that there may be issue related to more household crowding and children being more vulnerable and thus susceptible to infections.

Agam Rao, MD, FIDSA: I'll add that surveillance in DRC isn't as good as it is in the U.S. Only ~8% of cases are laboratory confirmed and many are based on clinical suspicion. We know preceding this outbreak that VZV and mpox were commonly confused with each other in DRC. We also know that concurrent outbreaks (e.g., measles) in some jurisdictions can complicate classifying cases as mpox. We don't think spread to children would occur the way it has occurred in DRC because many of the exposures in children there are due to direct contact with wildlife (i.e., the reservoir for mpox in endemic countries). It's not clear whether household transmission is really the reason for the many cases in children.

33. There are reports of TPOXX resistance, what is the status on that?

Agam Rao, MD, FIDSA: Patty Yu will mention in her slide deck. I'll add that CDC has previously published results detailed 46 resistant cases and a new/recent cluster has been detected in multiple states (and the jurisdictions are aware). We are working on characterizing those better. At least some of the cases among these 50 are among tecovirimat naive individuals (i.e., people who acquired virus from someone in which it had already become resistant, possibly because of tecovirimat use).

Timothy Wilkin, MD: we are monitoring in STOMP as well.

34. Does the series need to be restarted if Dose #1 was given in 2022?

Agam Rao, MD, FIDSA: No. Regardless of the amount of time that has elapsed since the first dose, the 2nd dose can be given now. We aim to try to get the 2nd dose at ~28 days because that's the earliest time point that it can be given, and we want people to be fully vaccinated as soon as possible. But if a lot of time has elapsed since the first dose, patients get that 2nd dose now. It's never too late to finish the series.

35. Dose of mpox vaccine is 0.5ml SC at 0 and 28 days. I remember that there was an alternate option 0.1ml Intradermal to allow vaccinating more patients (5 patients vs one patient). Is Intradermal route still recommended?

Boghuma Titanji, MD, MSc, DTM&H, PhD: Intradermal and SC administration yield an equivalent antibody response, but intradermal dosing was used primary when a shortage of vaccine doses was a concern. Important to remember that intradermal vaccination is associated with scarring with cosmetic implications particularly in individuals with very melanated skin and was a deterrent for some returning to receive their 2nd doses of vaccine in 2022-2023.

Agam Rao, MD, FIDSA: Both were equally effective. We describe that in this recent publication:

https://www.cdc.gov/mmwr/volumes/73/wr/mm7320a3.htm?s_cid=mm7320a3_w

As this manuscript states, "Currently, an adequate supply of JYNNEOS vaccine is available; therefore, clinicians can preferentially administer JYNNEOS via the subcutaneous route, although previously administered intradermal vaccine doses were effective and should be considered valid doses and not repeated." So you can administer all of the vaccine doses via the subcutaneous dosing now that we are not in a shortage situation. You can still administer it intradermally, but because many clinicians are not experienced with this route, you may opt to preferentially administer the vaccine subcutaneously. This information is also on the CDC websites.

36. RITE AID is fading----will Walgreens offer Jynneos?

Meghan Pennini, PhD: The pharmacies listed were not an exhaustive list, there are others offering Jynneos. We expect Walgreens will be offering it as well.

37. We have heard from a number of our STD/HIV service providers, who provide the majority of JYNNEOS vaccinations across PA, having struggles purchasing vaccine through the private market, even under our Special Pharmaceutical Benefits Program through our Division of HIV. We do have a decent supply on-hand here in the state, but for some providers in the state who serve LGBTQ+ communities that are not enrolled with the Bureau of Immunizations, are there any recommendations for how we as the jurisdiction can support those providers in obtaining vaccine on the commercial market?

Meghan Pennini, PhD: I would recommend you reach out directly to the manufacturer, they should be able to work with you to ensure supply is accessible to those providers.

38. Has there been experience on tecovirimat use with Clades I and II in Africa?

Boghuma Titanji, MD, MSc, DTM&H, PhD: Unfortunately, tecovirimat access is very limited in Africa outside of clinical trials. There is, however, an ongoing trial in the DRC which is nearing completion, and which should provide an answer to your question in the near future.

39. Were the fatal cases of mpox treated with Tecovirimat?

Agam Rao, MD, FIDSA: Yes, most of them were. Most of the cases occurred in persons who were hospitalized for >6 months and received multiple courses of tecovirimat, VIGIV, and brincidofovir/cidofovir. Unless a patient's own immune system is optimized, the therapeutics typically are not helpful. They are only viristatic (not cidal) and many of the deaths have occurred in people with CD4 <50.

40. Is it advisable to go ahead and disseminate these revised tpoxx criteria? We have a meeting with our HIV providers across our jurisdiction this Friday.

Agam Rao, MD, FIDSA: Yes you can share the information. It won't go live until 6/10. But please feel free to acquaint providers with it. Thanks!

41. It is a shame the children and pregnant/lactating women are excluded from STOMP, when they can still get access through EA-IND. We need to re-think when we can include them.

Patty Yu, MPH: Children and pregnant/lactating individuals are eligible for tecovirimat through both STOMP and EA-IND, with primary access through STOMP for study follow-up and potential PK sampling.

Timothy Wilkin, MD: Children and pregnant women have always been eligible for STOMP!!!

42. How quickly will TPOXX be available for a patient through STOMP for a remote enrollment? Can STOMP be accessed over a weekend?

Timothy Wilkin, MD: We are working on weekend coverage. We don't have the infrastructure currently. Otherwise, it is overnight courier service.

43. Please clarify: is the current recommendation, especially with use of commercial Jynneos product, to administer via the subcutaneous route. I think the intradermal route was under EUA and vaccine shortage may not be an issue now?

Agam Rao, MD, FIDSA: Currently, an adequate supply of JYNNEOS vaccine is available; therefore, clinicians can preferentially administer JYNNEOS via the subcutaneous route, although previously administered intradermal vaccine doses were effective and should be considered valid doses and not repeated. This information was recently added to CDC websites as well. It is also in this recent publication:

https://www.cdc.gov/mmwr/volumes/73/wr/mm7320a3.htm?s_cid=mm7320a3_w

The EUA remains active, but you may prefer to administer the vaccine doses subcutaneously because more clinicians are comfortable with this route of vaccination.

44. Any new recommendations related to need to restart mpox vaccination series if 2nd mpox dose is delayed beyond a certain time interval?

Agam Rao, MD, FIDSA: Similar to most vaccines, regardless of the amount of time that has elapsed since a first vaccine dose, the second vaccine dose should be given. So even if the first dose was given in 2022, the second dose should be given now.

45. So, no recommendation to give a 3rd dose if 2nd dose was given 2+ years after 1st dose? Rare vaccines do require restarting series if one of the doses is delayed beyond a certain time period.

Agam Rao, MD, FIDSA: Correct. No additional doses for the community affected by this outbreak.