CDC/IDSA COVID-19 Clinician Call:

Diagnosis and Treatment of Respiratory Illness This Winter Season

October 9, 2021

Q&A

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1. **Is there going to be any reexamination of the contribution of aerosol vs droplet for influenza transmission?**

   I don't have this information off-hand but will look into it and follow up. (Dr. Garg)

   Oct. 15 update - *While CDC is continually examining evidence on modes of influenza transmission, current evidence supports that influenza viruses are spread from person to person primarily through close-contact respiratory droplet transmission. More information can be found on our website.* (Dr. Garg)

2. **With Influenza activity so low for the last season, how was the influenza strains to include in the vaccine selected?**

   In its role as a WHO collaborating center, CDC conducts year-round surveillance for circulating flu viruses and uses this and other data to assess population risk and to recommend the vaccine viruses to include in the vaccine production for both Southern and Northern Hemispheres. While the number of viruses available last season were lower than in typical seasons, all available data was used for strain selection. (Dr. Garg)

3. **Dr Fauci has described two new platforms for flu vaccines including mRNA (Pfizer) and a polyantigen vectored vaccine. When might these be approved for use in the USA?**

   At this time, we do not have information on when these vaccines might be approved for use in the U.S. (Dr. Garg)

4. **How can we differentiate the clinical manifestations of flu infection and COVID infection?**

   Influenza and COVID infection cannot be reliably differentiated based on clinical criteria alone. If an individual has symptoms consistent with an influenza-like illness, testing for both SARS-CoV-2 and Influenza A/B is recommended. (Dr. Azar)

5. **Why not always use quadrivalent flu vaccines i.e. why even offer trivalent vaccine?**

   This season, all available flu vaccines are quadrivalent. (Dr. Garg)

6. **How long is flu vaccine's antibody durability? And also any updates regarding universal flu vaccine?**

   Overall, waning effects have not been observed consistently across age groups and virus subtypes in different populations, and the observed decline in protection could be attributable to bias, unmeasured confounding, or the late season emergence of antigenic drift variants that are less well-matched to the vaccine strain. More info here under duration of immunity: https://www.cdc.gov/flu/professionals/acip/immunogenicity.htm (Dr. Garg)

7. **For patients symptomatic with ILI, what is sensitivity of day 1, day 3, day 7 test for influenza and for COV-2?**

   The sensitivity of molecular/PCR tests for both influenza and SARS-CoV2 is very high in the first week after symptom onset (for COVID usually >95%). (Dr. Azar)

8. **Do you have data or reference about co infection with flu and COVID: worse or no difference?**

   So far there is very limited data on co-infection with flu and COVID other than case reports. There is really not enough data at this point to know if co-infection is more severe- but we will be monitoring for coinfection closely this season and collecting data on clinical course/severity of coinfections. (Dr. Garg)

9. **Can you please review interpretation of discordant results in a symptomatic person (e.g., positive antigen and negative NAAT) collected at the same visit?**

   NAAT is considered the reference standard test and so a positive antigen test and a negative NAAT test performed on the same patient on the same day is suggestive of a false positive antigen test. However, there inappropriate specimen collection for the NAAT specimen may lead false negative results. In a symptomatic patient, such a discordance may warrant a third test as a tie break but you also want to consider testing for other viruses (influenza, RSV and other) and bacteria as appropriate. (Dr. Azar)

10. **Any changes in recommendation on ideal timing of influenza vaccination in the US this year, given delay/low southern hemisphere rates thus far?**

    At this time, no changes to recommendation. Ideally vaccine should be administered in September or October, and ideally no later than the end of October. However, vaccine should continue to be administered for long as there is local circulation. (Dr. Garg)

11. **Would the co-administration of vaccines need to be in different sites (i.e. different arms)?**

    CDC recommends that vaccines that may be more likely to cause a local reaction should be administered in different arms if possible. If given in same arm, injection sites should be separated by at least 1 inch. (Dr. Azar)

12. **Are still to presume that in children over age 3 yrs., Strep throat is very uncommon when sore throat is accompanied with runny nose, runny eyes and cough, so that throat culture is NOT clinically indicated? And under age three years, throat culture also NOT clinically indicated. Or should TC be obtained when sore throat associated with URI findings or when throat appears red with exudate?**

    The IDSA recommends that clinicians make decisions on testing for GAS based on overall clinical symptoms and exposure history rather than a specific set of criteria (Centor or other). I am adult ID doc so less familiar with testing approaches for children but I do think that testing for GAS makes sense in children who have a sore throat/pharyngitis in addition to other URI symptoms. (Dr. Azar)

13. **Isn't it true that multiplex and singleplex tests can be "approved" as laboratory-developed tests (LDTs) under a clinical laboratory's CLIA license rather than as FDA-EUAs?**

    That is my understanding. (Dr. Azar)

14. **How does the BD Veritor CLIA waived testing for COVID-19, RSV, Strep and Influenza compare with the tests you chose to present?**

    It is an Antigen based test that is provides results in around 15 minutes. Antigen tests are generally less sensitive than PCR based tests. (Dr. Azar)

15. **Is there a viral therapy to treat RSV? I am not familiar with that?**

    Ribavirin is an antiviral that is a treatment option for bone marrow transplant patients with RSV. (Dr. Azar)

16. **Were there any differences between the molnupiravir responder patients and the molnupiravir non-responders in the study? (e.g presence of immunosuppression, age, etc)?**

    I have not seen granular data on this, only what Merck has released in press releases.

17. **Why is there not yet an accepted widely available antibody assay to determine adequacy of neutralizing antibodies, similar to chickenpox or measles? This is needed by front line clinicians to bring some rationality to discussions with individual patients around immunity/vaccine boosters etc.**

    Because we do not have a "serologic correlate of protection" for COVID. The same situation exists for other infections such as whooping cough. (Dr. Chatterjee)

18. **Does the vaccine or natural infection induce mucosal IgA antibodies?**

    SARS2 infection causes mucosal IgA (Jennifer Gommerman and colleagues, among others). We and other measured IgA in blood as a surrogate (Dan et al. Science, as one example). The RNA vaccines do not elicit a substantial IgA response. But IgG gets transferred into mucosal sites. This is the basis of the outstanding success of the HPV vaccine (papillomavirus). It is a vaccine that only elicits IgG and is > 99% effective at preventing mucosal infection. (Dr. Crotty)

19. **This information seems to suggest that the primary series could be robustly protective (without booster shots) - please comment**

    Current data suggests the currently approved or authorized COVID-19 vaccines are highly effective against hospitalization and death for the Delta variant within the first 6 months from immunization https://www.cdc.gov/coronavirus/2019-ncov/science/science-briefs/fully-vaccinated-people.html (Dr. Goswami)

20. **Current commercial antibody tests measure which type of antibody?**

    Depends on the test. Many measure RBD (a fragment of Spike), but some measure nucleocapsid (N, or NC). Nucleocapsid antibodies are irrelevant for protection. (Dr. Crotty)

21. **Do you have any paediatric data on T cell responses?**

    It is an important topic, but it is hard to get sufficient blood samples donated to make those measurement. I don't recall any published data on this. (Dr. Crotty)

22. **After infection, there is some data suggesting higher levels of antibody against spike in vaccinated but higher levels in RBD domain in unvaccinated. Does vaccine change the character of immune response?**

    Both the Pfizer and Moderna vaccines elicit higher RBD and Spike titers than is elicited in most infected persons. (Dr. Crotty)

23. **How does the immunological get affected by delta variant?**

    The immune memory generated by the Pfizer and Moderna vaccines recognizes Delta variant very well. (Dr. Crotty)

24. **Is the IgA deficient individual more susceptible to SARS-CoV-2 infection?**

    I am not aware of data on this. The RNA vaccines do not elicit a substantial IgA response. But IgG gets transferred into mucosal sites and can be protective. This is the basis of the outstanding success of the HPV vaccine (papillomavirus). It is a vaccine that only elicits IgG and is > 99% effective at preventing mucosal infection. (Dr. Crotty)

25. **If patient has covid-19, do they need booster dose?**

    While primary series vaccination decreases risk of future infections in people with prior SARS-CoV-2 infection, efficacy of a booster dose for fully vaccinated people with known prior SARS-CoV-2 infection is not yet known. (Dr. Goswami)

26. **If we are treating hospitalized and severely ill patients with immune suppressing meds (dex, to i, bari) during the proposex "inflammatory phase" what does this say about whether evidence of cell mediated immunity is reassuring?**

    Timing matters. It is a complex topic. Discussed at some length here:

    https://linkinghub.elsevier.com/retrieve/pii/S0092867421000076 (Dr. Crotty)

27. **For CDC: By when do you anticipate the Pfizer vaccine standing order template being updated with booster recommendations and posted?**

    We are aiming for within the next 7-10 days. (Dr. Goswami)

28. **Several hcw's have had 'breakthrough' infection prior to booster- can we assume that these people have some additional protection with antibodies from their breakthrough infection? (likely a Delta due to geographic location)**

    Previously infected persons who get vaccinated (at least one dose) have fantastic immunity, higher than that of normal vaccinated individuals. I summary this "hybrid immunity" in a short article in Science: https://www.science.org/lookup/doi/10.1126/science.abj2258. And there is now epidemiological data also. (Dr. Crotty)

29. **Are there any special considerations or concerns about a healthcare worker receiving a Pfizer booster in the third trimester?**

    There appear to be no safety concerns or special considerations for a Pfizer booster for pregnant women in the third trimester. (Dr. Chatterjee)

30. **Will those in the approved age groups no longer be considered fully vaccinated if they do not get the 3rd dose?**

    Administration of an additional dose to people with moderate to severe immune compromise or a booster dose is not required to be considered fully vaccinated for public health purposes. (Dr. Goswami)

31. **Are there ACOG and ACIP recommendations for 3rd doses pregnant women who have received Pfizer?**

    These will be included in updated CDC recommendations, to be posted hopefully this week https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html (Dr. Goswami)

32. **Such a small sample size to test a booster (11 and 12 ppl).**

    The Pfizer safety dataset on boosters involved 329 people and there was immunogenicity data on about 200 of these individuals. This was completely consistent with the guidance provided by FDA for the evaluation of boosters in this setting. (Dr. Marks)

33. **Can the panel comment on the fact that the mRNA vaccines might well be a 3 dose regimen? Also, the recent data from JNJ suggests it is a two dose and not a one dose vaccine. How are those decisions made?**

    The initial dosing schedule was decided by the sponsors based on animal studies. Dosing regimens for vaccines are sometimes revised based on emerging data after they become widely used, e.g. Trumenba, HPV. (Dr. Chatterjee)

34. **To the presenters: please comment on how you feel that we as a community of clinicians and scientists can trust the impartiality and science-based actions of the advisory committees and entities establish to ensure the safety and science-based implementation of vaccines if these past few days seem to be driven by political interactions.**

    If you watch the VRBPAC meeting, it will become clear that the committee members debated vigorously and each individual came to their own conclusions regarding the data presented. (Dr. Chatterjee)

35. **With the current knowledge can be projected how often we are going to need booster after third dose?**

    We do not know this yet. (Dr. Chatterjee)

36. **For the newly submitted Pfizer data on children ages 5-11, are there meetings for VEBPAC scheduled, and if so, when?**

    A VRBPAC meeting for this population is not yet scheduled, but please stay tuned. (Dr. Marks)

37. **I do not understand the word "waning immunity" if the pathogen changed from 6/8 months ago- delta is different, and we may have seen same levels of protection last fall rather than what was seen against the less transmissible and less severe D614G... no?**

    Two large studies in the UK were able to compare immunity to Alpha and Delta in the same time window, and found that, for example, the Pfizer vaccine was still very effective against Delta compared to Alpha. (Dr. Crotty)

    https://www.medrxiv.org/content/10.1101/2021.08.18.21262237v1

https://www.nejm.org/doi/10.1056/NEJMoa2108891

Effectiveness of Covid-19 Vaccines against the B.1.617.2 (Delta) Variant

38. **How does the composition of the booster dose differ from that of the first two doses/initial vaccine?**

    It is the same. (Dr. Chatterjee)

39. **Should booster doses for HCWs become optional versus obligatory?**

    The current CDC recommendation for healthy HCW less than 65 is that they MAY receive booster, not that they SHOULD or are required to receive. (Dr. Goswami)

40. **For CDC: When do you anticipate the updated booster recommendations being published in the MMWR?**

    The MMWR will be taking a few weeks to come out. In the interim we are aiming to update CDC Clinical Considerations within ~72 hours https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html (Dr. Goswami)

41. **People who had MIS-C after COVID-19 infection or vaccine, is a contraindication to receive the first/second dose vaccine or the booster vaccine?**

    No, although caution should be exercised - please see more specific guidance on MIS-C and COVID-19 https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html (Dr. Goswami)

42. **Is there evidence that booster vaccines have reduced risk of asymptomatic spread by people that have been given the 3rd dose. This would give additional reason for booster doses in healthcare workers and congregate settings.... etc.**

    Good question - no data yet. (Dr. Chatterjee)

43. **So if patient is on criteria for booster but got infected with the virus. Is booster still necessary?**

    While primary series vaccination decreases risk of future infections in people with prior SARS-CoV-2 infection, efficacy of a booster dose for fully vaccinated people with known prior SARS-CoV-2 infection is not yet known. (Dr. Goswami)

44. **What do you recommend for hospital administrators- should they MANDATE the booster dose for healthcare workers (physicians, nurses, etc.)? What data should they share with their staff, other than the weaning immunity?**

    No. (Dr. Goswami)

45. **What about if you are vaccinated then get infected**

    While primary series vaccination decreases risk of future infections in people with prior SARS-CoV-2 infection, efficacy of a booster dose for fully vaccinated people with known prior SARS-CoV-2 infection is not yet known. (Dr. Goswami)

46. What is holding the science of measuring protective immunity back? Accuracy? Reliability?

It is hard in many ways. One practical aspect is that measuring T cells is much more resource and time intensive than antibodies. At least 10x. So no COVID-19 correlates of protection study ongoing has been measuring T cells, only antibodies. (Dr. Crotty)