

Responses to Unanswered Questions Asked During the Webinar – Update 2022: COVID-19, Multisystem Inflammatory Syndrome in Children, and the Heart

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1. Are there any MIS-C data for children under 1 year of age?

There have been cases of MIS-C in children <1 year of age. However, the numbers are small; at the end of January 2022, children <1 year of age accounted for only 3.3% of 6,851 cases of MIS-C reported to the CDC.

2. What is the difference between “Long-COVID” in kids and MIS-C?

Both “Long-COVID” and MIS-C are forms of post-acute sequelae of COVID-19 (PASC). There is no agreed-upon definition of long-COVID, though generally it is persistence or new symptoms that develop after acute COVID-19 infection; some studies use persistence of symptoms >30 days while other studies have used persistence of symptoms >90 days after COVID-19 infection; the majority of children with long-COVID do not require hospitalization. On the other hand, MIS-C has a case definition published by the CDC; as part of that definition, children need to be sick enough to be hospitalized.

3. Recent CDC data suggest that new onset diabetes may be increased post-COVID. Will the MUSIC Study capture any data on this?

Yes; as part of our annual follow-up, we ask about the development of diabetes.

4. Are you aware of any new drug treatment trials underway for MIS-C?

At this time, I am not aware of drug trials for new medications to treat MIS-C. However, I know that there are randomized medication trials underway to determine potential best therapies in MIS-C.

5. What do you think contributes to the disparities in MIS-C in Black and Hispanic children?

I wish I knew the answer to this; I suspect part of the disparities in MIS-C relates to access to care. There may also be genetic differences that we do not yet fully understand.

6. Are the rates you presented in your talk calculated using a denominator of all vaccines or vaccines in the specific age group?

I believe this question is being asked regarding the Vaccine Adverse Event Reporting System (VAERS) reporting rates of myocarditis by age group? If so, I believe it is per age category.

7. Are MUSIC Study patients consented for individual-level genomic studies and are there plans for genomic sequencing in these studies?

Yes; it is an optional part of the study, but for those that consent, we collect a blood or saliva sample to perform whole genome sequencing in the future.

8. What are your thoughts on vaccinating after MIS-C?

I follow the CDC's stance on COVID-19 vaccination; namely vaccination is recommended in those to whom the vaccine is available based on age; however, patients should wait at least 90 days from MIS-C hospitalization. In those that had evidence of cardiac involvement (decreased function/squeeze of the heart, elevated troponin levels, arrhythmia suggestive of myocardial involvement), I wait until all cardiac testing is normal, including a cardiac MRI.

9. Can you comment on the thrombosis risks associated with MIS-C, known predictors, and best prophylaxis practices?

COVID-19 in general has been thought to lead to a hypercoagulable state. There was a pediatric study (Whitworth et al, "[Rate of thrombosis in children and adolescents hospitalized with COVID-19 or MIS-C](#)", *Blood*, 2021), which showed that MIS-C was an independent risk factor for thrombotic events in children with COVID-related illness. Children with MIS-C have an incidence of thrombotic events of 6.5%. Other predictors of thrombotic events in COVID-19 related illness was age \geq 12 years old, having cancer, and having a central venous line.

Unfortunately, we do not know the current best practices for thrombosis in MIS-C patients. There are some consensus statements based on expert opinion (one statement is from a group of pediatric hematologists and ICU physicians, another is from a group of pediatric cardiologists), but nothing like data driven recommendations. Most children are often put on aspirin, and if there are risk factors (like age), prophylaxis with low molecular weight heparin.

10. Do you discharge young adults (age > 18) with severe left ventricular (LV) dysfunction with an external defibrillator/LifeVest while waiting for LV function to improve?

I personally have never had a patient with MIS-C who had severe LV dysfunction at hospital discharge; most had normalized by the time of hospital discharge. So, unfortunately, I cannot speak about this specific scenario in MIS-C.

11. Have you seen COVID encephalitis that led to coma? How long did it take for improvement and treatments to be recommended?

I have not personally seen COVID-19 encephalitis; therefore, I cannot speak to this.

12. Do you think the aneurysms in MIS-C can be compared with aneurysms in Kawasaki Disease (KD) in terms of long-term outcomes?

It is hard to say at this point. The majority of aneurysms are small and resolve/normalize within months. This makes us hopeful that the mechanism of coronary involvement in MIS-C may just be hyperinflammatory state leading to dilation. However, large/giant aneurysms have been described, though they are quite rare; these large/giant aneurysms make us concerned of a mechanism similar to KD of a necrotizing arteritis.

13. [Yonker et al., 2021](#), showed that in children with MIS-C, a prolonged presence of SARS-CoV-2 in the gastrointestinal tract led to the release of zonulin, a biomarker of intestinal permeability, with subsequent trafficking of SARS-CoV-2 antigens into the bloodstream, leading to hyperinflammation. Is there any insight into preventing this?

This same author published a series of 4 patients in which a zonulin antagonist was used as an adjuvant therapy in MIS-C (see below). However, I am not aware of other studies.

- Yonker LM, Swank Z, Gilboa T, Senussi Y, Kenyon V, Papadakis L, Boribong BP, Carroll RW, Walt DR, Fasano A. Zonulin Antagonist, Larazotide (AT1001), As an Adjuvant Treatment for Multisystem Inflammatory Syndrome in Children: A Case Series. Crit Care Explor. 2022 Feb 18;10(2):e0641. doi: 10.1097/CCE.0000000000000641. PMID: [35211683](#); PMCID: PMC8860335.

14. MIS-C appears to be a hurricane that gives you 3-6 weeks to prepare. How should we prevent serious disease during that period after a COVID-19 infection or exposure?

We unfortunately do currently do not have any known therapies proven to prevent the development of MIS-C once a COVID-19 infection/exposure has occurred. We only have vaccination and other methods of prevention against contracting COVID-19 as the only prevention against developing MIS-C.