William Raszka, MD FAAP, UVM MC

There have been several reports of COVID-19 and severe inflammation in children that have been heavily publicized in media outlets in the last couple of days. The reports are showing an association with COVID-19 and syndromes consistent or similar to the Kawasaki disease. We have known that some adults with severe COVID-19 have had marked inflammation. When you measure inflammatory markers in some of these adults, they are just off the wall. They have really high levels of IL-6, IL-10, IL-12, VRP, etc. Because of the hypothesis of a cytokine storm in the critically ill adult, that is the rationale for using IL-6 inhibitor therapy (e.g. tocilizumab). This is approved for the treatment of rheumatoid conditions in children and adults, and is part of our pathway here at UVM MC for adults with severe disease.

However, last Sunday the PICU alert network in the UK released a memo to their members of an uptick in children with multi-system inflammation in association with COVID-19. NHS also reported a small uptick in Kawasaki-like disease in London hospitals. Children were young, 6 to 9 years of age and had a lot of abdominal complaints but many had cardiac inflammation. Once the announcement was made, many other public health authorities and hospitals in Europe reported similar findings. This was linked epidemiologically with COVID-19, though not all patients had a confirmed infection. It was also a subject of discussion with WHO earlier this week.

Where are we today? Italy has reported an increased number of cases of Kawasaki disease. One physician in Bergamo stated they had 20 cases during the time when they would expect to see 3-6, and a few tested positive for COVID-19. We do not know anything beyond that. France also reported an increase in patients with Kawasaki disease-like illness. As of this morning, they reported about 15 cases. Kawasaki disease is much more common in people of Asian descent and there are no reports in Asia. The UK has around roughly 19 patients. There have been some anecdotal reports in the U.S. over the past week. In NYC, a rheumatologist at Columbia reported 3 children who tested positive had signs of significant inflammation. National Children’s reported a couple of cases, and CHOP stated maybe, retrospectively, they had a couple of cases.

There are about 50 to 100 cases worldwide of children with some epidemiologic link to COVID-19 and cardiac inflammation. We do not know what the true link is as some are PCR antibody positive but many are not. So far there are no fatalities. There has only been one case reported that will be coming out in Hospital Pediatrics of a 6-month old who had typical signs and symptoms of Kawasaki disease and had mild respiratory complaints. Due to the delay in testing, the 6-month old was diagnosed with COVID-19 at discharge. 13,000 children have been diagnosed with COVID-19 to date. At this point in time, we do not have an explanation. Because of the COVID-era we are in now, things are being picked up pretty quickly. Anecdotal reports are important but there are no peer review lit and research yet.

Practice Issues - COVID-19 Testing in Vermont
Benjamin Grebber, LCOM MD Candidate Class of 2021

The new pediatric HAN added on April 21, 2020 noted the priority for testing symptomatic children with mild to moderate disease should be given to children of health care providers, with chronic underlying medical conditions, in congregate housing, and with exposure to a patient with COVID-19. During Commissioner Levine’s call yesterday, April 29, 2020, he discussed ramping up to 1,000 tests per day. Commissioner Levine outlined a three wave plan. Starting out mostly with people who are mildly

*Note: This is a paraphrased synopsis of the call and is not a word-for-word transcription.
symptomatic, health care personnel, residents in long-term care facilities, and corrections facilities and staff. In wave two, they would like to start testing people who are having procedures done as outpatients as well as individuals working in home health and hospice, and first responders. Lastly, in wave three, testing will be related to individuals in inpatient settings as well as anyone else in contact with children such as childcare providers, and individuals in quarantine.

Right now, we are currently offering a number of testing platforms in the State of Vermont. The testing platforms vary on times between 3.5 hours to 24 hours from receiving the samples. All of the tests provided are for nasopharyngeal (NP) testing only. However, as of this week, we received approval to do nasal swab testing in symptomatic patients. UVM laboratories had looked at Abbott ID Now Nasal testing and according to Harrington et al. (2020), they found 75% positive agreement and 99% negative agreement between ID Now Nasal swabs vs. NP Standard. As of this morning, the UVM lab has been in discussion about using saline for testing kits which would allow for the production of an additional 15,000 kits this week. They are ramping up production as well. We have not looked at any specific saliva tests yet but will look more into this as more data and research comes out.

We have created a recommendation list for what we should do in the future in terms of serology testing. As of right now, we have concluded and provided recommendations that testing is not sensitive and specific enough. The presence of antibodies does not confer “immunization passport.” We are not sure what these antibodies mean and it may not offer protection from recurrence. There is also lots of differentiation between the tests. These tests would be better for epidemiological studies and sero-prevalence across Vermont, rather than a yes or no answer to determine if an individual has had COVID-19. We are planning to meet again and reassess the data.

Questions/Discussion

C: These are small numbers but they could be significant if there is cardiac inflammation.
A: William Raszka, MD, UVM Children's Hospital & Larner COM Department of Pediatrics: All have done well.

Q: Should that change considering testing for kids with abdominal complaints?
A: William Raszka, MD, UVM Children's Hospital & Larner COM Department of Pediatrics: I would be cautious if they only had abdominal complaints. These children had adnominal complaints, and fever, and many of them had rashes as far as we can tell. So they just didn’t have abdominal complaints. They had signs and symptoms that overlapped with toxic shock and Kawasaki disease, so they were ill.

Q: Would you use the current recommendations to isolate if it is a negative test but clinically seems consistent or highly suspicious?
A: William Raszka, MD, UVM Children's Hospital & Larner COM Department of Pediatrics: If the pretest probability is very high and the NP test is negative, we continue precautions.
A: Benjamin Lee, MD, UVM Children's Hospital & Larner COM Dept. of Pediatrics: On the inpatient side, we did make a recommendation to use clinical suspicion in this decision-making and not rely solely on a single negative test.

Q: Were the kids with inflammation symptoms under 5? Were any older?
A: William Raszka, MD, UVM Children's Hospital & Larner COM Department of Pediatrics: Interestingly, children of all ages, which is a bit unusual for classic KD. Many were up to 9 and Italian reports, even saw teens.
C: Thanks. Triage just got more complicated...good to know!
A: William Raszka, MD, UVM Children's Hospital & Larner COM Department of Pediatrics: It is complicated; and, the CDC released six new symptoms. However, the six new symptoms do not include GI issues.

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Q: Can you clarify the testing of HCW in wave 1. Are those symptomatic HCW or totally asymptomatic HCW?
A: Ben Grebber, LCOM MD Candidate: In phase 1 testing, right now, the Governor is looking to test all people who are symptomatic who are health care workers.
A: Breena Holmes, MD, VDH: This is a rapidly changing story, but, yes, the health care workers who are asymptomatic will probably start to be tested in the context of reopening our hospitals for elective procedures.

Q: Do we have any data yet on sensitivity and specificity of any of these tests? Especially for people that are asymptomatic, how do we interpret these test (not the antibody tests, but the nasopharyng)?
A: Benjamin Lee, MD, UVM Children’s Hospital & Larner COM Dept. of Pediatrics: This is still not great data regarding sensitivity, although with more experience, it does seem the cases that are real-world sensitivity is perhaps lower than initially believed (meaning everyone is seeing a certain number of false negatives). For symptomatic patients, specificity can be considered to be quite good, meaning a positive result can be trusted. However, there are far less data for asymptomatic patients. Part of the challenge is differentiating those who are pre-symptomatic vs. those who remain asymptomatic.

Q: Any thoughts on the recent study showing (purportedly) that saliva tests are more sensitive than NP swabs? (Obviously a lot less unpleasant to obtain.)
A: Breena Holmes, MD, VDH: The saliva test information is circulating with our lab folks today. Stay tuned.
A: Paul Parker, MD, Richmond Pediatrics: https://www.medrxiv.org/content/10.1101/2020.04.16.20067835v1 (saliva study)
A: Ben Grebber, LCOM MD Candidate: We haven’t looked into tests right now in regards to saliva testing. There is some data out there, but right now the UVM lab is only doing NP testing as well as VDH. Eventually we’ll be offering the nasal swab. We’ll look into the saliva testing as more data comes out.

Q: With regard to the pediatric cases in the state, are there any communalities, length of illness recovery times, etc.? Were all exposed to an adult with COVID positivity prior to diagnosis?
A: Wendy Davis, MD, VCHIP: As a reminder, we have one pediatric case in the 0-9 age group, who is 5 years old and 18 in the 10-19 age group. Most of them are at in the upper half of that age spectrum.
A: Breena Holmes, MD, VDH: VDH has been doing analysis of death and they have been looking at different sub-populations, but they have not looked at that group of 15-19 year olds in our positive category. However, with increased testing we are going to have increased pediatric positive cases and we can then ask for more detail on those cases in terms of symptoms.
A: William Raszka, MD, UVM Children's Hospital & Larner COM Department of Pediatrics: I do not know much about the pediatric patients. To the best of my knowledge, all have done well and none hospitalized.

Q: If anterior nares samples, would we not need full PPE?
A: Breena Holmes, MD, VDH: That's right, no need for full PPE.

Q: Has there been any further word on CDC actually categorizing presumptive +‘s in the epidemiological tracking?
A: Breena Holmes, MD, VDH: The Vermont epidemiology team decided that they are not going to report on presumptive positives because we’re doing so much testing.

Q: With lower sensitivity, how would that impact schools opening in the fall and in particular what is going to happen at UVM?
A: Wendy Davis, MD, VCHIP: There was a bit of information released from the president of UVM and they anticipate opening with some in person classes in the fall and probably some online for those who don’t
feel comfortable attending in person. The plans are still in development and there is a task force working on this.

A Breena Holmes, MD, VDH: If you are talking about the public schools’ system, it is a daily ongoing conversation. We’re definitely opening schools in the fall and how we do that safely is a topic of great interest.

Q: What are your thoughts on COVID toes with negative test results?
A: William Raszka, MD, UVM Children’s Hospital & Larner COM Department of Pediatrics: We really do not know much about COVID toes. If the NP is negative, I would assume the patient does not have the virus in the nose or pharynx and would not isolate.
A: Benjamin Lee, MD, UVM Children’s Hospital & Larner COM Dept. of Pediatrics: If there were no other symptoms, I probably would not use COVID toes alone as criteria.
C: I propose that COVID toes is due to kids at home in bare feet and getting true perniosis and is unrelated to COVID. Put on socks, keep your feet dry.
C: Anecdotally, I have a patient with chilblains/perniosis for years and is having many flares and much worse symptoms this year with the unseasonably cold weather.