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Q&A: Discussion on COVID-19

Latest COVID-19 Insights from Doctors + Stories from the Frontline to inform Childhood Cancer Families & the General Community

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Hosted by: Solving Kids' Cancer

GENERAL INFORMATION

- The Centers for Disease Control and Prevention (CDC) website addresses many common questions people may have about COVID-19: *https://www.cdc.gov/coronavirus/2019-ncov/faq.html*
- The World Health Organization (WHO) website holds useful information, as well: *https://www.who.int/emergencies/diseases/novel-coronavirus-2019*
- Information and responses below are subject to change based upon a rapidly evolving pandemic. Please consult with your child's primary medical team for any and all medical advice and your child's hospital for its up-to-date hospital policies regarding COVID-19.
- Please understand that not all respiratory symptoms are due to SARS-CoV-2, the virus that causes COVID-19. Currently at Nationwide Children's Hospital, rhinovirus (common cold virus) and metapneumovirus are very common. However, if your child exhibits fever, cough or shortness of breath (current screening symptoms for COVID-19), then he or she will likely be tested for SARS-CoV-2.

DURING OR AFTER CHILDHOOD CANCER TREATMENT

1. **I am wondering about kids who need to travel for their clinical trials. Have the travel restrictions and compromised patient situation caused kids to drop out of clinical trials?**
   To date, children on clinical trials continue to be treated on study, as long as they do not meet off-study criteria specific to that study. Your child may not have to come to the clinic as often for certain testing, but that is specific to the study and a decision by your child's primary medical team. Be assured that patient safety remains the first priority for all children enrolled on any clinical trial. That said, most clinical trials are on hold for new accruals unless considered potentially life-saving.

2. **My son is a brain tumor patient in NY. His last MRI on March 9th indicated he needs another surgery/craniotomy. Thankfully the enhancement is very small (~0.7 cm), near the skull and not considered "urgent" by the neurosurgeon, however, I am becoming concerned about how long the delay will be for his surgery — What are people doing in these situations?**
   We would recommend that you contact your child's primary oncology team to determine next steps, as they know your child and his treatment course the best. Be reassured that medical decisions and needed care will not necessarily be "put on hold" due to COVID-19.

3. **Are kids who were on chemo at higher risk?**
   Yes, but most kids on chemo were already in some form of social distancing and thus have had less chance of being exposed to the virus. So far, we and other children's hospitals aren't seeing many kids on chemotherapy getting diagnosed with COVID-19.

4. **When a child has a suppressed immune system, do they still have the ability to mount an inflammatory response to the COVID-19 virus, causing all of the problems that are responsible for the respiratory issues?**
   Great question, and the answer is Yes. As an example, a child with profound neutropenia can still mount a fever response, and therefore needs to be admitted to the hospital for fever and neutropenia. The reason for this is that the immune system is redundant, which means a "next man up" back-up system is at play. Specifically, immune cells and the chemicals that they release can be activated by different signals or challenges to the immune system. Furthermore, they can be activated at different times after a challenge to the immune system.

   Could it be a protective factor in that case?
   Definitely, having redundancy in the immune response is a life-saving feature. The issue is that once activated, our immune systems have "turn off" switches, or regulatory cells and signals, that shut down the activated cells. As if we didn't have these "policeman" immune cells, our activated immune cells would act as "rioters" and cause havoc to our bodies. Therefore, certain drugs target specific immune cells or cytokines that they produce to shut down the immune response. Tocilizumab, a drug that blocks a

pro-inflammatory cytokine called interleukin 6, is used to treat “cytokine storms” associated with the use of certain immune cell therapies as well as after certain medical conditions.

5. **How far out can we safely delay follow up visits for kids in the first 5 years coming off ALL treatments? (The child in question is 3 years OT.)**
   Although such decisions are best made with you and your child’s primary medical team, a child that is off-therapy would likely have his/her visit deferred at this time unless he/she has developed clinical symptoms of concern. Most relapses occur in the first two years after therapy is discontinued, but are usually associated with clinical symptoms or signs of concern.

TREATMENTS FOR COVID-19

1. **If aggressive management is done from the onset of apparent infection, does it mitigate some of the detrimental infectious processes?**
   Response to COVID-19 is a continuum, starting with asymptomatic carriage and progressing to mild and then severe disease. The majority of persons with COVID-19 will experience mild to moderate symptoms. We are also learning that in many cases there may be no symptoms at all, though such individuals can still spread the infection to others. We are starting to define patient populations who are at higher risk for severe COVID-19, defined as requiring hospitalization or intensive care. Such risk factors include adults with underlying cardiovascular and lung diseases and diabetes. Immunocompromised patients also are at higher risk.

   Preliminary Estimates of the Prevalence of Selected Underlying Health Conditions Among Patients with Coronavirus Disease 2019 — United States, February 12–March 28, 2020

   Aggressive supportive care is the standard of care at this time, but for those patients that have severe disease, we are challenged to reverse the course given the lack of established antiviral therapies.

2. **Please comment on the recent accelerated FDA approval of chloroquine for COVID-19.**
   Yes, great question. As reviewed on the webinar with respect to vaccine development, the FDA is fast-tracking certain treatments deemed for accelerated use in patients. Please review the FDA letter for hydroxychloroquine as well as the statement on accelerated approval. Please remember that this is not the same as granting the drug conventional “FDA approval,” as such would require that the drug has been proven safe

and efficacious for that clinical indication. Also such “fast-track approvals” are rarely applicable for pediatric patients, as you will read in the FDA letter.

3. **Are there other drugs that our community is working on that you’d like to shine a light on instead?**
   Remdesivir is likely the current front-runner drug for COVID-19. However, data is pending from early phase trials. Remdesivir is currently available through an expanded access treatment protocol (NCT04323761), which means that the company may be able to provide drugs as long as the patient meets advanced disease criteria (compassionate use). Of note, the age criteria for this trial is ≥18 years. Other antivirals are in the early stage of development at this time.

4. **What trials are available for COVID-19 patients in Ohio or Columbus?**
   There are two clinical trials using Remdesivir for moderate (NCT04292730) and severe COVID-19 (NCT04292899) that are available at some centers in the US. Ohio centers will be participating soon. You can refer back to the website for updates. Both have age criteria ≥18 years.

   The ClinicalTrials.gov website is a resource to look for updated clinical trials. Of note, at this time, most trials for COVID-19 are either observational (no treatment) or not available in the US.

5. **Has it been identified, what percentage of the tests are false negatives?**
   Great question! We want “screening tests” like the PCR test that detects SARS-CoV-2, the virus that causes COVID-19, to be very sensitive to detect the virus (“true positive” result) and very specific to detect only that virus (“true negative” result). When a screening test fails to detect the virus, then we call the result a “false negative.” When a screening test is positive but not from the virus, then we call the result a “false positive.” As there are different screening tests being used, the sensitivity and specificity for each varies. Therefore, the false negative rates also vary according to the screening test used. But we want the sensitivity and specificity of a screening test to be as close to 100% as possible.

NSAIDS

1. **Is there really a problem with administering NSAIDS in the case of fever (as long as the platelet levels are sufficient) for fever/pain? (If so, this seems counterintuitive, since the problem is an inflammatory response in the body, creating the respiratory problems.)**
   As long as the child has good kidney function and platelet levels, then NSAIDs are permissible to take. One needs an inflammatory response to get rid of any infection. We normally call that inflammatory response an immune response, as inflammation is needed to rid the body of infections.

   However, the immune response needs to ultimately be regulated or shut off; so the immune response doesn't cause harm to the body. Yes, local inflammatory responses to infection can cause more harm than good. In the case of COVID-19 pneumonia, the virus is in the lungs, and the immune response is causing inflammation in the lungs.

   In some individuals, the immune response may be overreacting, by recruiting more immune cells that release more inflammatory chemicals that cause further fluid to build up in the lungs. How to separate the "super producers" from "normal producers" of an immune response is not possible at this time. That said, we do know that viral loads are very high in the lungs. So there's lots of virus for immune cells to try and eliminate in the lungs.

   The WHO has since reversed its position not to use ibuprofen.

2. **Please advise. I would assume the results they are referring to where NSAIDS were detected, must have been in patients who were already in end organ failure due to hypoxia and the NSAIDS did additional damage to the kidneys, correct?**
   Good point, but hard to say as we don't know when the NSAID exposure occurred.

3. **Please advise. Many of the medications that our kids on chemo take are rough on the liver and NSAIDS seem like the better, more effective approach to symptom management.**
   Acetaminophen depletes glutathione stores in the liver, which are needed to keep the liver healthy. Some chemotherapy agents also cause liver toxicity through the same mechanism. Therefore, avoiding "additive effects" of damage to the liver seems prudent.

TESTING FOR COVID-19

1. **Is there anywhere to see numbers of positive cases, normalized to the number of tests being done?**
   Not to our knowledge, as such data would require a pool of all test results performed. South Korea is the country having utilized the most testing.

2. **Are individuals who donate blood tested or simply "screened" for COVID19?**
   Yes, blood donors are screened by symptoms prior to blood donation. The American Red Cross has an informative webpage on the blood donation process.