PIONEERING DIAGNOSTICS

LEARNING LOUNGE EXCLUSIVE : DIAGNOSING AND TREATING GI INFECTIONS WITH AN ANTIMICROBIAL STEWARDSHIP PERSPECTIVE

Viewpoints Series:

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In patients with gastroenteritis, quickly identifying the causative pathogen can prevent inappropriate antimicrobial use and help reduce costs associated with intensive imaging procedures and isolation protocols. Additionally, unnecessary antimicrobial use can disrupt the gut microbiome and further aggravate gastrointestinal (GI) infections. Syndromic testing can provide fast, accurate results across a range of causative agents. In this article, Stephen Vella, PhD, discusses the challenges of managing various GI infections while following antimicrobial stewardship practices with Dr. Jillian Cotter, Assistant Professor of Pediatric Hospital Medicine at Children's Hospital Colorado Anschutz Medical Campus.

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bioMérieux: What advice would you give to healthcare providers who want to improve their antimicrobial stewardship practices while treating GI infections?

Cotter: This is a great question. I think diagnostics stewardship is really key in this case. We need to do a better job of integrating the utilization of molecular diagnostics with clinical decisions. Combining these two approaches together would contribute to improving antibiotic stewardship. At Children's Colorado, we are interested in studying the clinical impact of a multiplex panel as compared to our standard of care. In an ongoing diagnostic stewardship study, we found that the benefits of multiplex panel utilization included sending less tests down to the lab, getting results back quickly, and attaining high detection rates post-implementation when compared to the previous standard of care. I think the key is determining the predictive values used to identify children who are most likely to have a bacterial or parasitic pathogen and to test early and often, while reducing the amount of testing on other children who are less likely to have a bacterial or parasitic pathogen.

bioMérieux: In your experience, which GI pathogens are often overlooked or misdiagnosed?

Cotter: I think we are still learning risk factors for *C. difficile*. Not a lot of providers see *C. diff* all the time and might be surprised by a true *C. diff* result. If the patient presenting symptoms has recently traveled and has bloody and/or prolonged diarrhea, these symptoms are indicative for ordering PCR testing to rule out other types of infections.

I would say that bacterial infections like *Salmonella* and *Shigella* are often overlooked or misdiagnosed. *Salmonella* can cause some pretty bad bacteremia along with gastroenteritis, so I think people are often surprised when they get a positive *Salmonella* result. Not everyone needs to be treated when they have a *Salmonella* infection, but we do need to think about a patient's risk for bacteremia in comparison to how sick they are and when treatment is actually warranted. Prescribers also need to be careful about not giving antibiotics for certain types of *Shigella* and/or *E. coli* infections.

bioMérieux: According to the WHO, norovirus ranks as the number one cause of foodborne illness globally[1] and is categorized as a GI infection. With the lifting of COVID-19 restrictions, norovirus outbreaks have increased in several parts of the world.[2,3] What can healthcare professionals (HCPs) do to successfully diagnose rising numbers of norovirus?

Cotter: From an epidemiological perspective, it can be useful to track outbreaks and potentially inform future vaccine work. I think it's like that for all respiratory viruses, and GI viruses are similar. If we, as healthcare professionals, can limit contact with other people, the rates of these types of infections will decline. As we open back up and start activities that would enable transmission through the fecal/oral route, norovirus is likely to spread, especially in daycare facilities.

bioMérieux: Returning to the subject of *C. difficile*, why is it especially difficult to detect in children[4] and how does this impact pediatric antimicrobial use?

Cotter: *C. diff* is very challenging in kids due to asymptomatic colonization. This presents a particular challenge for multiplex PCR testing. There are some studies where a percentage of healthy children were detected to be positive for *C. diff*, even when they had no symptoms. Therefore, in a patient that is one year of age, your pretest probability for *C. diff* is fairly low. We know that colonization rates are particularly high in younger children, especially children under the age of two. If you perform a full multiplex panel and detect *C. diff*, then it's hard to know what to do, because it is difficult to ignore a positive *C. diff* result. At the same time, they probably do not actually have infectious *C. difficile*.

This is important to note because it contributes to rising rates of antibiotic use in young kids when they probably didn't need antibiotics to begin with. This overprescribing can cause unintended side effects, such as adverse reactions to antibiotics, and it can also contribute to the rise of antibiotic resistance (AMR) within our society.

That is why we need to use our pretest probability and ask ourselves if the patient has risk factors for *C. difficile*. This is difficult for providers to do because we don't see a significant amount of *C. diff*, so clinical decision support tools that can help providers understand a patient's risk for *C. diff* can be super helpful.

bioMérieux: How does multiplex PCR testing support antimicrobial stewardship regarding the diagnosis and treatment of *C. difficile*?

Cotter: In adult patient care, I think doctors often start antibiotics empirically and afterwards order a multiplex stool test to determine when to deescalate antibiotic use. As doctors, we often assume most GI infections in children are viral and tend not to start antibiotics preemptively before getting test results.

Some hospitals have made great efforts to promote diagnostic (and thus antibiotic stewardship) by offering a multiplex panel with and without *C. difficile*. This enables the provider to utilize the advantages of a multiplex PCR panel in conjunction with the pretest probability to detect *C. diff*. Additionally, many hospitals limit results for kids under the age of one, which helps to promote antimicrobial stewardship.

bioMérieux: What about for the diagnosis of parasitic infections?

Cotter: I think anyone traveling to endemic places and/or experiencing bloody or prolonged diarrhea would warrant checking for parasites. That is where the multiplex panel really is incredible, because you used to wait for typically 3 days for the results of the assays to come back. Usually, the patient was either already recovered or was significantly worse, so from the perspective of GI parasitic infections, multiplex PCR is awesome. When I get a virus positive result, it reaffirms what I thought clinically.

What I think we need in the future of multiplex panels is a way to better predict who is most likely to benefit clinically from the results. We can then steer our diagnostic stewardship efforts toward improving who gets tested based on the individual patient's predictive probability of an actionable result.

bioMérieux: How can HCPs best utilize isolation protocols for patients with suspected GI infections in order to slow the spread of antimicrobial resistance (AMR)?

Cotter: There are two schools of thought in the inpatient setting. At Children's Hospital Colorado, we isolate anyone who has symptoms of vomiting or diarrhea, regardless of whether the multiplex is positive or negative. On the other hand, the second school of thought is that you isolate based on positive or negative results; a practice that other hospitals have implemented.

For example, if there was a *C. diff* outbreak, isolating kids to prevent the infection from spreading would reduce the number of antibiotics that we use overall. Knowing this information can assist in preventing contagious kids from going out into public spaces, like schools or daycares, and exposing friends and other people in the community. If you have an infection that is confirmed to be positive, staying home can be especially beneficial, as we have experienced during the COVID-19 pandemic.

Daycare protocols themselves make it challenging with GI infections. In many areas, a doctor's letter must be obtained or antibiotics started for 24 hours before returning to the facility. These types of protocols just breed complication from an antibiotic resistance perspective, as they motivate providers to prescribe antibiotics to parents as a means to get their kids back into daycare. It presents a vicious cycle.

bioMérieux: At what point in the patient care journey is it most effective to introduce molecular testing for suspected GI infections?

Cotter: In the inpatient setting, there are robust studies showing that community-acquired GI infections are very uncommon in children who have been hospitalized for more than two days. Therefore, testing

after the first two days of hospitalization is very low yield – meaning that it is very unlikely to detect anything that could lead to an actionable result. I would say testing early in this case is important. The earlier you test, the more likely you are to respond to that result and use it to dictate additional treatment, start treatment, reduce the type of treatment, and/or impact the length of stay — all of which can also have significant cost implications for the patient and their family to consider.

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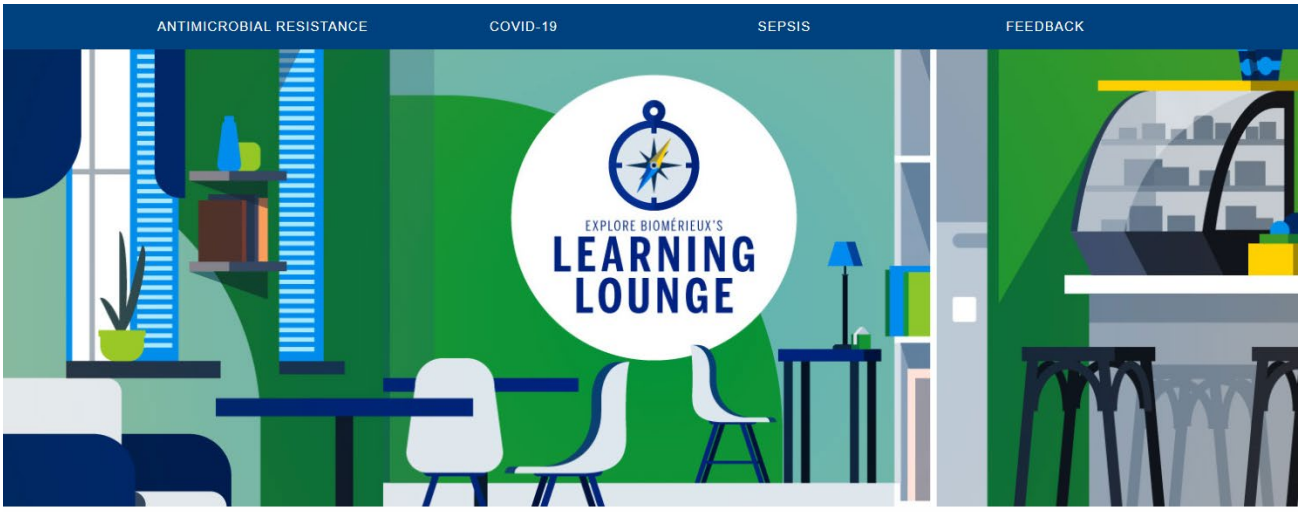

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