# FilmArray GI: findings from first months of clinical use

## Anne Ford

April 2016—Treating *Clostridium difficile* can be dreadfully difficult, even when a clinician doesn't have to navigate ordering restrictions based on testing frequency. So when Julie A. Ribes, MD, PhD, director of clinical microbiology at UK HealthCare in Lexington, Ky., received a phone call last year from a clinician who asked for repeat *C. difficile* testing, she was more than sympathetic.

Dr. Ribes

"We deal with these issues all the time," said Dr. Ribes in "How Syndromic Testing Can Improve Patient Care," a November 2015 webinar produced by CAP TODAY in collaboration with BioFire Diagnostics. "We have these testing frequencies that are established, and so the patient's been treated and the patient got better, and now the patient is sick again, and [the clinician says] 'Your computer is not letting me order my test.'" They talked about the persistence of DNA, and Dr. Ribes suggested the patient might have something other than *C. difficile* infection.

To find out, she ran BioFire's Film-Array gastrointestinal panel. "The patient actually had been secondarily infected with rotavirus," Dr. Ribes said. "So this patient was then not re-treated for *Clostridium difficile*, despite the fact that the panel also was positive for *C. difficile*. But it was within that 21-day period following adequate treatment, and so this patient was just managed for rotavirus."

That's just one of several success stories Dr. Ribes reported in the webinar, which she co-presented with Jennifer Dien Bard, PhD, of the Department of Pathology and Laboratory Medicine at Children's Hospital Los Angeles and of the University of Southern California's Keck School of Medicine. (See the May issue for Dr. Dien Bard's discussion of the meningitis/encephalitis panel.)

In the webinar, Dr. Ribes, who is also a professor of pathology and laboratory medicine at the University of Kentucky College of Medicine, shared her experiences with the Film-Array GI panel during its first seven months of clinical use last year in her laboratory. Before implementing the panel, her laboratory relied on routine stool culture using a variety of selective and nonselective media to detect what Dr. Ribes calls "the usual suspects"—*Salmonella, Shigella*, and the like.

"We certainly had the ability to pick up *Campylobacter* and *E. coli* O157:H7 and a variety of other organisms," she said. "Several different bugs, however, needed to have special requests from our clinicians due to the low rate at which we were seeing them." *Yersinia* and *Vibrio*, for example, required add-on tests. "*Campylobacter* is kind of a miserable growing organism," she pointed out. "And so there was no stool culture before its time."

Also available: a comprehensive ova and parasite, which could detect helminth eggs and larvae and pathogenic and nonpathogenic protozoa. Again, if clinicians wanted other tests, such as a modified acid fast for *Cyclospora* or *Cystoisospora* or a modified trichrome for the detection of microsporidian species, those had to be added on. As for viruses, "We had a rotavirus EIA that was available on the day shift, and we had a viral culture that would go on for 21 days," she said. "Herpes viruses, adenovirus, or enterovirus could be picked up with our viral culture. And then, in addition to that, we had the opportunity to do some send-out testing," such as PCR for Norwalk virus.

BioFire's FilmArray GI panel offers the following diagnostic analytes: bacterial targets *Campylobacter* species, *C.*

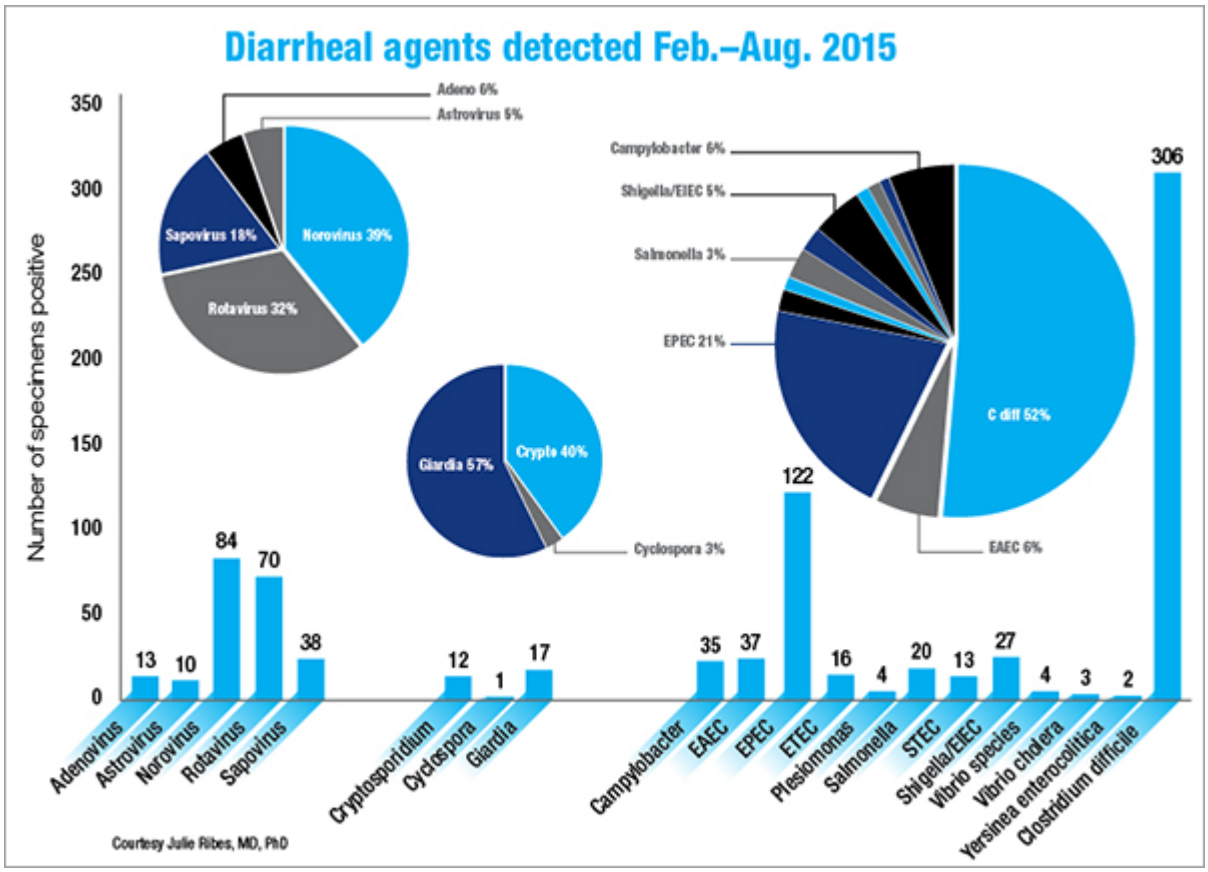
*difficile, Plesiomonas shigelloides, Salmonella* species, *Yersinia enterocolitica*, and *Vibrio* species; diarrheagenic *E. coli/Shigella* targets enteroaggregative *E. coli*, enteropathogenic *E. coli*, enterotoxigenic *E. coli*, Shiga-like toxin-producing *E. coli*, and *Shigella*/enteroinvasive *E. coli*; parasitic targets *Cryptosporidium, Cyclospora cayetanensis, Entamoeba histolytica*, and *Giardia lamblia*; and viral targets adenovirus F 40/41, astrovirus, norovirus GI/GII, rotavirus A, and sapovirus I, II, IV, and V.

When deciding whether to adopt the panel, Dr. Ribes and her staff found themselves attracted to what she called its "one-stop shopping" capabilities. "It covers all the big players, even if the ordering physicians aren't really thinking about them," she pointed out. "It gives us a turnaround time of within hours, versus the three to four days that would be required for us to culture the organisms or to have send-out testing."

Then, too, the panel replaced the routine stool culture bench ("which eliminated half a tech of effort every day") and eliminated some send-out testing as well as the stool EIAs that went along with the culture platform. In addition, it was cost-effective for the patient as a bundle. "The cost was established at such a level that our patients would not be penalized for our moving to this new technology."

The new panel presented potential downsides, the first of which pertained to *C. difficile*. "Do you retain the standalone test? . . . Do you stay with a *Clostridium difficile* individual assay for hospitalized patients? And . . . what [do] you do with the kids who are under three who have *C. difficile* detected?" Dr. Ribes asked.

In addition, her laboratory is located in a community that sees significant foreign travel and is home to an international adoption clinic, meaning that "a complete ova and parasite cannot be entirely replaced," she said. "If you're looking for worms, eggs, microsporidia, etc., this panel is not going to be helping you to look for them."




She and colleagues also knew that targeted culture was going to continue to be needed. "So even though we were planning on abandoning culture, we couldn't abandon it entirely. And it was valuable to me that we continue to send out isolates to the state laboratory for epidemiologic purposes." They also needed to be able to provide susceptibility testing for *Shigella* isolates. "Our pediatricians were requesting this, and so we needed to retain the ability to automatically and reflexively establish cultures at UK HealthCare. The PCR can remain positive for a very long period following clinical cure, and so the test of cure still needs to be culture-based.

“And then, what about *Aeromonas* species, which are not included in this panel? If we had requests specifically to look for *Aeromonas*, we still needed to have the ability to do that.”

Finally, the cost of the new panel to UK HealthCare was higher than the cost of the routine bacterial culture for reagents.
Nonetheless, the laboratory decided to discontinue its routine stool culture in favor of the comprehensive GI PCR panel. EIA use was discontinued, and frequency limits were set at q seven days for negative and q three weeks for positive. Retesting of patients with a single event of diarrhea was not necessarily encouraged, but clinicians were able to have additional testing performed at defined frequencies.

“We retained the ability to perform targeted culture for susceptibility testing for epidemiology and for test of cure, and we retained a routine ova and parasite DFA and modified acid fasts for special patient populations,” Dr. Ribes explained. “We retained viral cultures specifically for CMV and HSV with the understanding that we could also isolate adenovirus and enterovirus, and we retained our *Clostridium difficile* PCR standalone testing for our hospitalized patient populations in whom we were thinking primarily about *Clostridium difficile*.”

Dr. Ribes remembers the first few days after going live with the new panel in February 2015 as a time of great excitement. “By the time the first weekend was over, we had three noroviruses, four rotaviruses, and a *Clostridium difficile*,” she recalled. “And that Monday after our first full week of testing, one of my technologists was in the elevator and overheard the pediatricians talking about the comprehensive GI panel and how cool it was, and she proudly announced that she worked in the laboratory and knew exactly what they were talking about.”

In the first seven months, the laboratory performed the new panel 250 to 300 times per month, with positive patients representing about 30 to 35 of those (“far and away above what we had seen prior to that time,” Dr. Ribes said). *C. difficile* represented about 37 percent of pathogens detected, while non-*C. difficile* bacteria represented about 34 percent, viruses about 26 percent, and parasites about three percent.

“The viruses were mostly those that we really were not able to detect prior to this time or that clinicians weren’t ordering the tests on,” she clarified. Those were predominantly rotavirus, norovirus, and sapovirus. In parasites, *Cryptosporidium* and *Giardia* were predominant. And in bacteria, 52 percent were *Clostridium difficile*, with enteropathogenic *E. coli* as the next largest group at 21 percent.

Further analysis showed that 81 percent of patients had a single organism identified through use of the panel, 16 percent had two, three percent had three, and 0.2 percent had four or more. “When we take a look at which of the analytes were present in these mixed cultures, you can see that adenovirus, sapovirus, *Cryptosporidium*, or one *Cyclospora*, and the enteroaggregative *E. coli*, enterotoxigenic *E. coli*, and *Vibrios* really rounded out the ones that were seen most commonly in mixed culture.”

Further benefits quickly showed up in the form of patient success stories. For example, “We had a physician who called in saying, ‘We really think we’ve got a *Vibrio cholerae*,’” Dr. Ribes said. “This was a kid from South America. Lo and behold, it was positive for *Cyclospora*. The clinician had not ordered an ova and parasite, and so this would have been missed in this case.”

And then there was the outside facility whose housekeeper came to work ill with vomiting and diarrhea. Before long, other workers were experiencing the same symptoms, and “we were able to capture specimens, identify the fact that this was norovirus, and implement infection-control procedures to make sure the facility was cleaned and people were deferred from working and that the clinic reopened only after the infection-control intervention was successful,” she said.

Dr. Ribes expressed pride, too, in the case of a positive *Vibrio cholerae* patient. The panel was positive for *Vibrio*, and they were able to isolate the *Vibrio*. “A second patient, not too distant from this first one, came up positive by the panel, and yet we were unable to isolate the organism.” Both panels were reported to the Department of Health. The second patient was interviewed, and it was found that both patients had been to Haiti and that the patient lacking a culture isolate had been on an aircraft on which other passengers had vomited and had diarrhea.

“We felt that this was a true case, and it would not have been identified had we been using our standard culture techniques.”

Dr. Ribes’ takeaways for those who choose to implement the BioFire Film-Array GI panel: Think about your disclaimers up-front, and consider what course of action to take for patients under age three who test positive for *C. difficile*. “Do you report the results? Do you report them with a disclaimer? What happens if your panel tells you that you have *Shigella*, but we aren’t able to culture it? What are you going to do when your clinicians are expecting susceptibility testing?” Think, too, about how you’re going to report the requirement for containment and other comments.

And it’s “tremendously important,” she concluded, to “plan adequately and do a lot of training” and ongoing education of clinicians to ensure the most effective use for this panel.

*Anne Ford is a writer in Evanston, Ill. The webinar “How Syndromic Testing Can Improve Patient Care” can be viewed via captodayonline.com at* http://j.mp/syndromictest.