THE PATHCARE NEWS

Molecular diagnostic panel improves the diagnosis of infective diarrhoea

Although few gastrointestinal infections may require specific therapy, the quick and efficient detection of a causative agent of diarrhoea may limit unnecessary use of antimicrobials, reduce hospitalisation duration and also provide valuable information regarding epidemiology and infection control.

Traditionally the diagnosis of infective diarrhoea was made by stool culture, while microscopy enabled us to identify parasites such as *Cryptosporidium* sp., *Giardia* and the eggs of nematodes and trematodes. Lateral flow assays are also available to detect enteric viruses but these lack sensitivity and specificity.

Culture is mainly geared towards the detection of pathogenic bacteria such as *Salmonella* and *Shigella* species. The identification of diarrheagenic *E. coli* is difficult, as these organisms form part of the normal stool flora and additional tests need to be performed to confirm toxin production. Other pathogens that are difficult to detect by culture include *Yersinia*, *Campylobacter* and *Vibrio* species, as these require specific culture techniques.

Pathcare is now introducing a more comprehensive molecular panel to diagnose infective diarrhoea, which includes 7 bacteria, 4 parasites and 5 viruses of importance in gastrointestinal infections (See table 1).

 **BACTERIA**	 **PARASITES**
Campylobacter (jejuni, coli, and *upsaliensis)*	*Cryptosporidium*
Clostridium difficile (Toxin A/B)	*Cyclospora cayetanensis*
Plesiomonas shigelloides	*Entamoeba histolytica*
Salmonella	*Giardia lamblia*
Yersinia enterocolitica	
Vibrio (parahaemolyticus, vulnificus and *cholerae)*	
Vibrio cholerae	
Diarrheagenic *E. coli*/Shigella	 **VIRUSES**
Enteroaggregative *E. coli* (EAEC)	Adenovirus F 40/41
Enteropathogenic *E. coli* (EPEC)	Astrovirus
Enterotoxigenic *E. coli* (ETEC) lt/st	Norovirus GI/GII
Shiga-like toxin-producing *E. coli* (STEC) stx1/stx2	Rotavirus A
E. coli 0157	Sapovirus (I, II, IV and V)
Shigella/Enteroinvasive *E. coli* (EIEC)	

Table 1: Bacterial, parasitic and viral pathogens detected by the Biofire gastrointestinal PCR panel.

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When should this panel be requested?

- In vulnerable patients (e.g. the immune incompetent or the very young) a specific diagnosis of infective diarrhoea may be of value.
- When the specific identification of the causative agent of a gastro-intestinal infection will have therapeutic impact, i.e. by withholding antimicrobial therapy when a viral agent is identified, or when alternative agents need to be administered e.g. metronidazole for the treatment of diarrhoea caused by *Giardia lamblia*.
- When a difficult-to-detect organisms is suspected to be the cause of diarrhoea, e.g. *Giardia* or *Cryptosporidium*.
- When a quick result is desired – the turnaround time of this test will be less than 24 hours, while a culture may take up to three days, especially where a slow growing organism such as *Campylobacter* is involved.

Bear in mind that:

- There is a risk of false negatives due to the presence of sequence variants in the gene targets of the assay, amplification inhibitors in specimens, or inadequate numbers of organisms for amplification in the sample submitted.
- Nevertheless, the detection level of a molecular test such as this is very low and the detection of organisms that may form part of the normal faecal flora may not necessary indicate disease. A good example of this is *C. difficile*, which may colonise up to 20% of adults and even a higher percentage of neonates and children, and may therefore be an incidental finding in patients without typical antibiotic associated diarrhoea*. It is therefore important to correlate the results of this diagnostic panel with the history and clinical presentation of the patient.
- Multiple pathogens may be detected in one sample, and the therapeutic implications of these should be clinically determined.
- The test identifies *Campylobacter, Cryptosporidium* and *Vibrio* at the genus level and will not discriminate between different species. It is also set up to detect the most important of these species implicated in disease, and some rarer species of lower pathogenic potential may not be detected.
- The performance of the GI Panel has not been established in individuals who received vaccines. Recent oral administration of a rotavirus vaccine may cause positive PCR results in approximately 80% of individuals after the first dose and 50% of individuals after the 2nd/3rd dose, and is detected for approximately 2 - 4 weeks after administration. The recent administration of oral typhoid or cholera vaccines to travellers may also lead to positive results for these pathogens.

When should culture and microscopy still be requested on stool samples?

Culture and microscopy remain the cheapest way to detect bacterial pathogens such as *Salmonella* and *Shigella* species. Although less sensitive, microscopy may detect *Entamoeba hystolitica, Giardia* and *Cryptosporidium*. **Microscopy is still indicated to detect parasites not included in this panel (request parasite microscopy with concentration technique), and culture is still indicated if antimicrobial sensitivity testing is required for bacterial pathogens.**

*A separate PCR to detect toxin producing *C. difficile* is available (L3354).