Reply to Beal et al., 'The "3-Day Rule" for Stool Tests May Not Apply When Using PCR Panels'

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The letter by Beal et al. (1) raises a number of interesting points of discussion. Foremost, we compliment them on their recent publication accessing the use of a multiplex PCR panel for the detection of gastrointestinal pathogens (2). We agree that whenever there are significant technological advances, former tenets of practice should be examined for continued validity.

Beal and colleagues, in a review of their data, noted that 17% (41/241) of the specimens were submitted after 72 h of hospitalization. This raises several questions. Did diarrhea develop after hospitalization, were these repeat stool studies, or was a diagnostic opportunity missed upon admission? The last may occur when gastrointestinal symptoms are not the chief complaint and the review of the systems is inadequate. They report that six patients tested after 72 h of hospitalization had gastrointestinal pathogens detected by the multiplex PCR assay. Five of these patients had symptoms present on admission, but either another stool test was ordered (3 patients) or no stool studies were ordered (2 patients). We contend that if the multiplex PCR panel was used for these patients upon admission, then the pathogens could have been detected earlier, actually supporting the 3-day rule.

Our colleagues correctly point out the patient populations for which the 3-day rule should be relaxed (3, 4). It is for this reason we have allowed clinical providers to override our electronic intervention (5). Advances in informatics that will more thoroughly profile patients are needed, so that electronic interventions can be more specifically tailored to certain patient populations. Additionally, we fully agree with our colleagues that the development of evidence-based diagnostic algorithms are superior to a "shotgun" approach to test ordering but must point out that, ironically, these syndromic multiplex PCR panels represent a molecular "shotgun" approach and are not algorithmic in nature. This observation does not mean that we do not support the judicious use of such panels. As above, the inability to readily embed best-practice diagnostic test algorithms represents another shortcoming of current hospital and laboratory informatics systems.

Does the detection of all the pathogens present in a multiplex panel matter? This question was recently raised with respect to testing for respiratory viruses in immunocompetent children (6, 7). In the hospital setting, we believe that most medical professionals would rather know the cause of the gastroenteritis, even if targeted therapy is unavailable (e.g., for Norovirus). Conversely, payors have questioned the need for the detection of all the targets within these assays and contend that the added cost of detection has not changed the episode of care for individual patients, which in some instances may be true (e.g., proposed/draft local coverage decision DL37330 [8]). A provocative Point-Counterpoint manuscript examines both sides of the question of whether to restrict or make orders more widely available for these syndromic PCR panels (9).

Multiplex molecular assays usually cost more than traditional microbiologic studies. As new tests that add cost are introduced, it is necessary to demonstrate added value.

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The value may be to the individual in the form of a better outcome or fewer unnecessary tests or procedures. Additionally, there may be value to the hospital in the form of decreased lengths of stay, better use of antimicrobial agents, and the opportunity to avert outbreaks through rapid detection and employment of effective infection prevention. Beal and colleague are complimented on the extension of their study beyond a simple analytical validation (i.e., the detection of pathogens). They evaluated potential impacts on antimicrobial stewardship, ancillary studies (e.g., radiologic imaging), and length of stay. These system-based cost reductions and enhanced quality of care are not being considered by payors, who simply refuse to reimburse because the agent detected did not have an actionable therapy. Knowing the pathogen, in scenarios such as these, likely does matter. In the absence of knowing the cause of disease, providers often continue to investigate, which becomes costly. This highlights the greatest opportunity in recent times for microbiologists, pathologists, and other clinical laboratorians to become more involved in the system-based aspect of evidence-based, value-driven health care delivery.

Finally, we conclude our reply as our colleagues concluded their letter: “more data are needed” to assess the validity of the 3-day rule in the era of syndromic molecular testing.

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