Shiga Toxin Antigen Detection Should Not Replace Sorbitol MacConkey Agar Screening of Stool Specimens

The interesting paper by Gavin et al., describing their experience using an enzyme immunoassay (EIA) to identify stools containing Shiga toxin (Stx)-producing Escherichia coli (STEC) (3), adds to the growing literature that non-O157:H7 STEC are overlooked pathogens. However, as physicians, clinical and public health microbiologists, and disease control epidemiologists, we are concerned by the authors’ use of an EIA to screen stools and, only if this test is positive, to then seek E. coli O157:H7 with sorbitol MacConkey agar culture (SMAC).

The promoted approach has several pitfalls. First, in a study which several of us coauthored, EIA was less sensitive than SMAC screening in detecting E. coli O157:H7 (5). We suspect that in vitro Stx production is not consistently above the level of detection by EIA. Particularly troubling is that E. coli O157:H7, the STEC with the strongest and most enduring association with epidemics and severe illnesses, might be overlooked unless EIA are complemented by parallel, and not sequential, culture. Second, while there is value in detecting infections caused by non-O157:H7 STEC, these organisms have lesser risks of precipitating the hemolytic-uremic syndrome (HUS) than do E. coli O157:H7, which are optimally identified using SMAC screening in parallel to, and not sequential with, the EIA. Providers need to know, as early in illness as possible, if a patient infected with an STEC has a high (i.e., those infected with E. coli O157:H7) or a considerably lower (i.e., those infected with non-O157:H7 STEC) likelihood of developing HUS (1). Even a 1-day delay in finding the agent producing the signal in the EIA can have considerable implications for clinical care (7). Third, because E. coli O157:H7 has a well-established association with outbreaks from common sources or exposures, it is critical that infecting organisms be forwarded to public health laboratories urgently, so that they can be genotyped (2, 6). Identifying the sources of epidemics of this high-profile pathogen could be slowed, or made impossible, by laboratory algorithms that employ SMAC only after an EIA on a broth culture produces a signal that suggests the presence of an STEC. Such delayed isolation of E. coli O157:H7 is inappropriate, considering its ability to cause outbreaks and life-threatening human illnesses.

We applaud the attempts by laboratories to find unusual and overlooked causes of human enteric infection, such as non-O157:H7 STEC; in fact, we encourage Stx antigen detection to accomplish this goal and note that there are circumstances where this methodology is more sensitive than culture alone for detecting the presence of E. coli O157:H7 (4). Unfortunately, however, a diminishing proportion of stools submitted for culture in the United States undergo SMAC screening (8). While Stx antigen detection by EIA should, intuitively, always identify E. coli O157:H7, there are insufficient data to justify eliminating SMAC screening in favor of EIA detection of Stx, and we are concerned that algorithms as proposed by Gavin et al. might lead to missed or tardy diagnoses, delay disease control interventions, and adversely affect clinical care and public health.

REFERENCES


Eileen J. Klein
Jennifer R. Stapp
Children’s Hospital and Regional Medical Center
Seattle, WA 98105

Marguerite A. Neill
Brown University School of Medicine
Providence, RI 02912

John M. Besser
Minnesota Department of Health
Minneapolis, MN 55414

Michael T. Osterholm
University of Minnesota
Minneapolis, MN 55455

Phillip I. Tarr
Washington University School of Medicine
Saint Louis, MO 63110

Authors’ Reply

Where’s the beef? It appears that Klein et al. and we agree that demonstrating the importance of non-O157:H7 STEC, the usefulness of a Shiga toxin assay in detecting diseased patients, and the clinical impact of detecting all STEC strains are the main goals of our paper (3, 5). We hope that our data and the comments of Klein and colleagues convince others to investigate the importance of STEC in their communities and consider using a Shiga toxin assay to detect serotypes other than O157:H7. No disagreements here.

Klein et al. raise the following questions. (i) Is culture using SMAC more sensitive for detection of O157:H7 serotype than a Shiga toxin assay? In our patient population they were equivalent. In contrast, the study by Klein et al. found SMAC to be more sensitive (5). This discrepancy may have resulted from differences in study design. In their study, Klein et al. included...
only pediatric patients, included specimens collected by rectal swabbing, and used a different Shiga toxin assay (5). Investigators disagree on the sensitivities of Shiga toxin assay and SMAC for detection of STEC. Kehl et al. reported superior sensitivity of Shiga toxin assay for detection of serotype 0157:H7 compared to SMAC (100 versus 60%, respectively) (4). Decisions can and should be made by local experts using local data. (ii) Is O157:H7 more pathogenic than other serotypes of STEC? In our 29 cases, patients were as likely to have severe disease regardless of serotype. In addition, non-O157:H7 serotypes were the etiologies in more than 50% of our patients. Similarly, reports from around the world document increasing prevalence and pathogenicity of non-O157:H7 strains (1, 2). In contrast, non-O157 serotypes were responsible for a small minority of disease in the pediatric population described by Klein et al. (5), again emphasizing differences among patient populations and the importance of local knowledge. (iii) Is a delay in culture of 1 day a clinical liability? We perform toxin testing daily, providing results to clinicians as quickly as, or more quickly than, SMAC culture. (iv) Is a delay of 1 day before the isolate is forwarded to the public health laboratory unacceptable? Our public health laboratory is notified the same day a toxin assay is positive. The O157:H7 strain would be forwarded the following day. At this time, our public health laboratory no longer accepts non-O157:H7 strains, will not accept Shiga toxin-positive stools negative for O157:H7 for testing, and is not open Saturday and Sunday. Thus, in practice, in our population, a 1-day delay introduced by sequential rather than concurrent culture is less important than other public health issues existing with reporting of this disease.

We appreciate the close scrutiny and thoughtful suggestions provided by Klein et al. Our screening strategy was shown to significantly expand the detection of adult and pediatric patients with infection caused by STEC. Whether this strategy is applicable in other populations must be determined locally, as stated in our discussion. Once again, we all agree that expanded, timely testing by more laboratories is needed and that a comprehensive approach to STEC testing should include a Shiga toxin assay. Whether or not a sorbitol MacConkey agar plate is used can be determined by local data and experts.

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