Shiga Toxin Testing for All Enteric Pathogen Requests on Stool

Background Information

Shiga toxin-producing strains of *E. coli* (STEC) are responsible for hemorrhagic colitis and potentially more serious complications, including hemolytic uremic syndrome (HUS) and death. The main sources of infection with STEC are contaminated raw or insufficiently cooked foods of animal origin, for example, meat and dairy products. Each year, STEC causes an estimated 73,000 cases of hemorrhagic colitis.[1,2] Approximately 38%-61% of individuals who are infected with STEC will develop hemorrhagic colitis; 5-10% of patients infected with STEC will develop HUS, and 10% of those who develop HUS will die or have permanent renal failure.[2]

Initially, a particular serovar, *E. coli* O157: H7, appeared to be responsible for the majority of cases of colitis and its consequences. Subsequent studies have reported that as many as 30%-50% of STEC infections are caused by non-O157:H7 *E. coli*, but common to these is the presence of a Shiga toxin.[3] Many serovars of *E. coli* that possess the Shiga toxin now have been identified, and these would be missed if one confines testing to detection of *E. coli* O157:H7 alone.

In 2006, the Centers for Disease Control (CDC) recommended that laboratories implement an assay that would detect all Shiga-toxin producing *E. coli* on all stools that are routinely submitted for routine enteric pathogen testing.[4] The STEC assays can detect two different toxins, described as Shiga toxin 1 and Shiga toxin 2. Toxin 2 is associated with a fourfold more likely chance for development of HUS and other complications, although both toxins have been associated with HUS.[2,5] Antibiotics should not be used to treat STEC infections, since this has been shown to increase the risk of HUS development.[6]

Clinical Indications

Diarrhea caused by enterohemorrhagic *E. coli* strains are most often seen in patients who acquire the organism in the community, not in the hospital. This is the same for other community-associated enteric pathogens such as *Salmonella* and *Shigella*. Patients who have been in the hospital for > 3 days when symptoms of diarrhea develop are likely to have *Clostridium difficile* enterocolitis and not enterohemorrhagic *E.coli*. However, in patients hospitalized because of bloody diarrhea and/or hemolytic uremic syndrome, testing for Shiga toxin is appropriate.

The presence of blood in stool samples always has been a potential marker for *E. coli* O157:H7, however, many patients with STEC infections will not present with bloody diarrhea.[7] Shiga toxin testing will be performed on all stool samples that are submitted to the Clinical Microbiology laboratory for detection of enteric bacterial pathogens regardless of whether the samples are bloody. Routine testing of these stools also includes culture for detection of *Salmonella* spp. and *Shigella* spp. and enzyme immunoassay for the detection of *Campylobacter jejuni*.

Reporting and Interpretation

Stool samples that are found positive for either Shiga toxin 1 or Shiga toxin 2 will be reported as positive for either or both. Samples that are negative will be reported as negative for both Shiga toxins. Shiga toxin 1 produced by *E. coli* is similar to the toxin produced by *Shigella dysenteriae* type 1 strains. Therefore the EIA may yield a positive result in patients infected with *S. dysenteriae* type 1 strains, however, the incidence of *S. dysenteriae* in the United States is very low.

Results will also include positive and negative findings for *Salmonella*, *Shigella*, and *C. jejuni*.

Reporting codes:

Positive for Shiga toxin 1
Negative for Shiga toxin 2

OR

Negative for Shiga toxin 1
Positive for Shiga toxin 2

OR

Negative for Shiga toxin 1
Negative for Shiga toxin 2

OR

Positive for Shiga toxin 1
Positive for Shiga toxin 2

Limitations of the Assay

This immunochromatographic assay is a qualitative assay and can not be used to determine any quantitative results. Test results should be used in conjunction with clinical information about the patient.

Shiga toxin 1 produced by *E. coli* and the toxin produced by *Shigella dysenteriae* type 1 strains are nearly identical. The immunochromatographic result of positive for Shiga toxin 1 could represent infection with either *E. coli* or *S. dysenteriae*. Culture will always be performed along with routine enteric pathogen requests. If *Shigella dysenteriae* were the producer of the Shiga toxin it should be positive in culture. Antibiotic treatment of hemorrhagic colitis due to *E. coli* is contraindicated since it may worsen the risk of hemolytic uremic syndrome; however, if *S. dysenteriae* is present, antibiotic treatment may be indicated.

All stool samples with a positive Shiga toxin result will be sent to the ODH for confirmation of the enteric pathogen as *E. coli* and to rule out the possibility of *S. dysenteriae*. In addition, our routine processing of the stool includes examination for *Shigella* spp,which is reported along with results of the Shiga toxin if it is found.

Methodology

The assay used in the Clinical Microbiology laboratory is an FDA-cleared commercial immunochromatographic rapid test that utilizes monoclonal antibodies that will complex with any Shiga toxin (1 and/or 2) antigen that is present in a broth-enhanced stool sample. A control area on the assay card is present for each sample, and results can only be reported for presence of the toxins if the control card is also positive.

References

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3. Johnson KE, Thorpe CM, Sears CL. The emerging clinical importance of non-O157 Shiga toxin-producing *Escherichia coli*. *Clin Infect Dis*. 2006;43:1587-95.
4. CDC recommendations for laboratory identification of Shiga toxin-producing *Escherichia coli*. 2006;55(28):1045.
5. Paton JC, Paton AW. Pathogenesis and diagnosis of Shiga toxin-producing *Escherichia coli* infections. *Clin Microbiol Rev*. 1998;11:450-79t.
6. Wong CS, Jelacic S, Habeeb RL, Watkins SL, Tarr PI.The risk of hemolytic uremic syndrome after antibiotic treatment of *Escherichia coli* O157:H7.infections. *N Engl J Med*. 2000;29:1930-6.
7. Gavin PJ, Thomson RB. Diagnosis of Enterohemorrhagic *Escherichia coli* Infection by Detection of Shiga toxins. *Clin Microbiol Newsl*. 2004;26:49-54.

Test Overview

Test Name	Routine stool culture and EIAs for enteric pathogens
Reference Range	Negative for Salmonella, Shigella, Campylobacter, E.coli 0157:H7 and Shiga Toxin
Specimen Requirements	Place 5 ml stool in Cary-Blair transport media immediately after collection. Transport at refrigerated temperature.
Stability (in Cary-Blair transport media)	Ambient: 1 hour; Refrigerated: 72 hours; Frozen: Unacceptable
Ordering Mnemonic	STOCUL
Billing Code	77142
CPT Codes	87045; 87046; 87427(x2); 87449

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