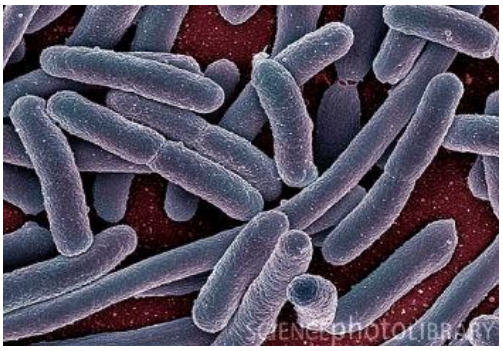
National Enteric Disease Surveillance: STEC Surveillance Overview

Surveillance System Overview: National Shiga toxin-producing *Escherichia coli* (STEC) Surveillance

Shiga toxin-producing *Escherichia coli* (STEC) are estimated to cause more than 265,000 illnesses each year in the United States, with more than 3,600 hospitalizations and 30 deaths (1). STEC infections often cause diarrhea, sometimes bloody. Some patients with STEC infection develop hemolytic uremic syndrome (HUS), a severe complication characterized by renal failure, hemolytic anemia, and thrombocytopenia that can be fatal. Most outbreaks of STEC infection and most cases of HUS in the United States have been caused by STEC O157. Non-O157 STEC have also caused US outbreaks. Although all STEC infections are nationally notifiable, for several reasons many cases are likely not recognized (2). Not all persons ill with STEC infection seek medical care, healthcare providers may not obtain a specimen for laboratory diagnosis, or the clinical diagnostic laboratory may not perform the necessary diagnostic tests. Accounting for under-diagnosis and under-reporting, an estimated 96,534 STEC O157 and *168,698* non-O157 infections occur each year (1). STEC transmission occurs through consumption of contaminated foods, ingestion of contaminated water, or direct contact with infected persons (e.g., in child-care settings) or animals or their environments.



Colored scanning electron micrograph (SEM) of Escherichia coli *bacteria.*

National STEC surveillance data are collected through passive surveillance of laboratory-confirmed human STEC isolates in the United States. Clinical diagnostic laboratories submit STEC O157 isolates and Shiga toxin-positive broths to state and territorial public health laboratories, where they are further characterized. State and territorial public health laboratories send reports of these STEC isolates electronically to the Centers for Disease Control and Prevention (CDC) using a variety of mechanisms. Data are collected into the Laboratory-based Enteric Disease Surveillance (LEDS) system, which is maintained by the Division of Foodborne, Waterborne, and Environmental Diseases (DFWED) in the National Center for Emerging and Zoonotic Infectious Diseases. Annual summaries of these data are the national source of serotype information for STEC. Unusual or untypable isolates or Shiga toxin-positive samples from which no STEC can be isolated by the state or territorial public health laboratory are forwarded to CDC's National *Escherichia* and *Shigella* Reference Laboratory in the Enteric Diseases Laboratory Branch (EDLB) in DFWED; results are reported back to the referring public health laboratory.

LEDS surveillance data on isolates are reported by state and represent the state where laboratory confirmation and subtyping occurred; the reporting state may not be the state of residence of the person from whom the isolate was obtained. Reports include basic demographic information, O antigen and H antigen data, and the clinical source of the specimen from which STEC was isolated. Reporting rates vary by state and year. The national

STEC surveillance data are dynamic; data from previous years may change as isolate reports are added or corrected. Because national STEC surveillance is laboratory-based, more than one isolate may be sent for a given patient or illness. Thus, more than one serotype may be reported for a given patient or illness, though in practice this occurs rarely. The number of isolates with incomplete and unknown O and H antigen data vary by state and year. As with any surveillance system, data reported to LEDS may have errors. Because the surveillance system is passive, some STEC identified in clinical laboratories may not be reported. LEDS surveillance data can include multiple isolates from a single illness in a patient; therefore, isolation rates are not equivalent to incidence rates.

Other sources of national-level STEC surveillance data

Several other CDC systems conduct surveillance for STEC infections. The National Notifiable Diseases System (NNDSS) collects and compiles reports of nationally notifiable infectious diseases, including STEC infections (3). NNDSS collects data from states on laboratory-confirmed and probable cases of STEC O157 (since 1996) and non-O157 STEC (since 2000). NNDSS data are collected from states by several mechanisms, including the National Electronic Diseases Surveillance System (NEDSS), which is under development; currently, laboratory-based information such as serogroup and serotype is not available from NNDSS. The National Antimicrobial Resistance Monitoring System (NARMS) monitors antimicrobial resistance among enteric bacteria including STEC O157 from humans (4). The Foodborne Disease Outbreak Surveillance System (FDOSS) uses the National Outbreak Reporting System (NORS) to collect reports of foodborne, waterborne, enteric person-to-person, and animal contact-associated disease outbreaks from local, state, tribal, and territorial public health agencies (5).

Laboratory Identification of STEC

Pathotypes of *Escherichia coli*

E. coli that cause diarrheal disease are categorized into six pathotypes based on virulence factors-- enterotoxigenic *E. coli* (ETEC), enteropathogenic *E. coli* (EPEC), enteroinvasive *E. coli* (EIEC), enteroaggregative *E. coli* (EAEC), and enterhemorrhagic *E. coli* (EHEC) (6,7). The term "enterohemorrhagic *E. coli* (EHEC)" is often used interchangeably with "STEC" and is intended to denote the subset of STEC capable of causing bloody diarrhea or HUS. However, because different definitions of EHEC have been used in the scientific literature, to minimize confusion, CDC uses "STEC." The term STEC is preferred for surveillance and is used in this summary because *E. coli* in this group can clearly be identified by their ability to produce one or more Shiga toxins or the presence of the genes encoding these toxins. Shiga toxins are also referred to as verocytotoxins (or verotoxins) and, accordingly, STEC can be referred to as VTEC (verocytotoxin-producing *E. coli*). All *E. coli* can be characterized by their major surface antigens, including somatic (O) antigens and flagellar (H) antigens. Serogroup classification depends on the O antigen only, whereas serotype is more specific, including both the O and H antigens. About 200 STEC serotypes have been recognized. Pulsed-field gel electrophoresis (PFGE) provides further subtyping within serotypes and is an important tool for identifying and investigating outbreaks.

Identification of Shiga toxin and virulence factors

The toxin produced by STEC was named based on its similarity in structure and function to Shiga toxin produced by *Shigella dystenteriae* type 1 (8). Identification of an STEC requires demonstrating that an *E. coli* isolate can produce one or more Shiga toxins or that it contains the genes encoding these toxins. However, all *E. coli* O157:H7 strains are considered to be STEC regardless of Shiga toxin testing results, because virtually all strains of this serotype produce Shiga toxin; negative Shiga toxin test results can occur if Shiga toxin genes are lost during infection or culture of the isolate. Shiga toxin (Stx), which is encoded by the *stx* gene, is the main STEC virulence factor. Stx1 and Stx2 are the two primary types of Shiga toxins. The presence of the stx_2 gene has been identified

as a risk factor for bloody diarrhea and HUS (9). STEC isolates characterized at the CDC Reference Laboratory are tested by polymerase chain reaction (PCR) for stx_1 and stx_2 genes, but the subtypes of these genes are not routinely assessed.

Before 1995, Shiga toxin was detected by using assays available only at reference and research laboratories. In 1995, the Food and Drug Administration (FDA) licensed the first of several enzyme immunoassays (EIA) for the detection of Shiga toxin. Use of these assays, and related lateral flow antigen detection assays at clinical diagnostic laboratories has greatly increased detection of non-O157 STEC infections.

All available isolate information should be submitted to national STEC surveillance (O antigen, H antigen, rough status [if appropriate], Shiga toxin genes [stx_1, stx_2] as well as any other virulence factors, if known).

Testing for STEC

Healthcare providers should notify clinical diagnostic laboratories when STEC infection is suspected so that appropriate testing methods can be applied. All stools submitted for testing from patients with acute community-acquired diarrhea (i.e., for detection of the enteric pathogens *Salmonella, Shigella,* and *Campylobacter*) to clinical laboratories should be cultured for STEC O157 on selective and differential agar. These stools should be simultaneously assayed for non-O157 STEC with a test that detects the Shiga toxins or the genes encoding these toxins. All STEC O157 isolates should be forwarded as soon as possible to a state or local public health laboratory for confirmation and additional molecular characterization (i.e., PFGE analysis and virulence gene characterization). Detection of STEC or Shiga toxin should be reported promptly to the treating physician, to the public health laboratory for confirmation, isolation, and subsequent testing of the organism, and to the appropriate public health authorities for case investigation. Specimens or enrichment broths in which Shiga toxin or STEC are detected but from which STEC O157 are not recovered should be forwarded as soon as possible to a state or local public health laboratory (10).

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