Shiga Toxin Producing *Escherichia coli*

Allen Bryan, MD, PhD[a], Ilan Youngster, MD[b], Alexander J. McAdam, MD, PhD[c,*]

KEYWORDS

• Shiga toxin–producing *Escherichia coli* • Enterohemorrhagic *Escherichia coli*
• *Escherichia coli* O157 • Gastroenteritis

KEY POINTS

- Infection with Shiga toxin–producing *Escherichia coli* (STEC) causes a range of manifestations, from asymptomatic carriage to hemorrhagic colitis and hemolytic uremic syndrome.
- The primary mechanism by which STEC damages humans is production of Shiga toxins, which inhibit protein synthesis.
- The main reservoir for STEC is the intestinal tract of cattle; transmission usually occurs by ingestion of contaminated foods.
- The most common serotype of STEC is O157:H7, but other serotypes also commonly cause human infections.
- Diagnostic testing for STEC can be performed by culture, immunoassays, and molecular assays; these tests differ in their sensitivities and specificities, and in their ability to detect all STEC or only those of the O157:H7 serotype.

INTRODUCTION

Enteropathogenic *Escherichia coli* are commonly classified pathotypically, by the patterns of manifestations observed in infection (**Table 1**). However, these descriptively useful terms can be subject to confusion, both from differences in exact case definitions, and from horizontal gene transfer between strains, which produces organisms causing infections with features fitting multiple classifications. Shiga toxin–producing *E coli* (STEC) is usually classified pathotypically as enterohemorrhagic *E coli* (EHEC). STEC is by far the most common type of EHEC, and so the 2 terms are sometimes used synonymously. This should be avoided, as Shiga toxins 1 and 2 (Stx1 and Stx2) can also be produced in strains with other characteristics consistent with enteroaggregative *E coli* (EAEC).[1–3] In this review, we briefly discuss the pathogenesis,

[a] Division of Laboratory Medicine, Department of Pathology, Beth-Israel Deaconess Medical Center, 330 Brookline Avenue, Boston, MA 02215, USA; [b] Division of Infectious Diseases, Boston Children's Hospital, 300 Longwood Avenue, Boston, MA 02115, USA; [c] Department of Laboratory Medicine, Boston Children's Hospital, 300 Longwood Avenue, Boston, MA 02115, USA
* Corresponding author.
E-mail address: alexander.mcadam@childrens.harvard.edu

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Table 1
Common pathotype classifications of *Escherichia coli* according to symptoms and infection site

Pathotype	Disease and Symptoms	Infection Site	Virulence Factors
Enterohaemorrhagic *E coli*	Watery diarrhea Hemorrhagic colitis Hemolytic-uremic syndrome	Distal ileum Colon	*stx*
Enteropathogenic *E coli*	Profuse watery diarrhea	Small intestine	*eae*, *bfp*
Enteroaggregative *E coli*	Watery diarrhea, traveler's diarrhea, endemic infection of children	Intestines	*aat* family
Enteroinvasive *E coli* (and *Shigella*)	Shigellosis/bacterial dysentery	Colon	*tpaH*, *ial*
Enterotoxigenic *E coli*	Watery diarrhea, traveler's diarrhea	Small intestine	Labile toxin, stable toxin
Diffusely adherent *E coli*	Diffuse, persistent watery diarrhea	Intestine	?

The strength of the associations between the pathotypes and the disease or symptoms varies.

clinical manifestations, and epidemiology of STEC, and then focus on the laboratory detection of STEC in more depth.

MICROBIOLOGY AND PATHOGENESIS

Terminology

The defining characteristic of STEC is the production of 1 or more of the extracellular toxins known as Stx1 and Stx2, Shiga-like toxins,[4] or simply Shiga toxins. An alternate name for these toxins is verocytotoxins,[5] derived from the reaction of Vero monkey kidney cells to the toxins.[6] Although it is placed in a separate genus, *Shigella* species are phylogenetically within the clade *E coli*.[7] The high relatedness of these organisms is believed to have facilitated transfer of the genes for Stx1 from *Shigella* species to *E coli* via lambda or related phages.[8,9]

Shiga Toxins

Stx1 is nearly identical to the *Shigella dysenteriae* toxin, differing by a single amino acid.[10,11] Stx2 was originally distinguished from Stx1 by neutralization by a separate antiserum.[12,13] Stx2 is exclusive to *E coli* and is found in numerous variants with only minor differences in amino acid sequence. All Shiga toxins are produced via a single operon containing at minimum the 2 genes *stxA* and *stxB*, and at least 1 promoter. The Shiga toxin operon(s) are embedded within the genomes of integrated lambdoid prophages.[14] They may be acquired by horizontal transmission via phage as well as by direct inheritance.[15]

Shiga toxins are AB5 toxins, meaning they are composed of a single copy of the ~32 kDa A component (produced by stxA), which bears the enzymatic activity of the toxin, and 5 copies of the ~8 kDa B component (produced by stxB), each of which bears 3 binding sites for the Shiga toxin receptor (**Fig. 1**).[16,17] The AB5 family additionally includes pertussis toxin, cholera toxin, and the labile enterotoxin of enterotoxigenic *E coli*.[18]