

# Traveler's diarrhea, a serious health threat in the world: a narrative review



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## Abstract

Traveler's diarrhea is one of the disorders of the digestive system and leads to abdominal pain and loose stools. This disease is caused by eating contaminated food and drinking contaminated water. When visiting a place that is different from the living environment of travelers in terms of climate, health standards, and social conditions, the possibility of contracting traveler's diarrhea increases. The most well-known gastrointestinal pathogen and the typical component of the microbiota in the human gut are *Escherichia coli*. Enterotoxigenic, enteroinvasive, enteropathogenic, and enterohemorrhagic *E. coli* are some of the designated pathotypes that are used to categorize the many types of *E. coli* that cause diarrhea. Each pathotype's strains have a unique collection of virulence-related traits that influence the clinical, pathological, and epidemiological aspects of the illnesses they cause. In this succinct overview, we highlight the important characteristics that set the different pathotypes of diarrheagenic *E. coli* apart. The development of logical strategies for the management and prevention of *E. coli*-induced diarrhea has been facilitated by our growing understanding of the pathogenic processes of these bacteria. Investigations investigating the virulence of *E. coli* are also helping to provide light on the history and development of bacterial pathogens in general. Although *Escherichia coli* is crucial for maintaining healthy gut physiology, this species also contains primary pathogens that are responsible for several different diarrheal illness syndromes. There are presently five unique kinds of diarrheagenic *E. coli* that exhibit diverse virulence traits, interact with the intestinal mucosa in various ways, induce different clinical syndromes, have different epidemiologies, and belong to different O: H serotypes. The most typical sickness among people who move from parts of the world with abundant resources to those with scarce resources is traveler's diarrhea. The anxiety of getting diarrhea, Traveler's diarrhea (TD) episodes are almost always self-limiting and benign, but the dehydration that can exacerbate an episode can be severe and pose a greater health risk than the actual illness. The purpose of this study, Provides an overview of *E. coli* and reviews the factors involved in diarrhea for clinicians.

**Keywords:** diarrhea, *Escherichia coli*, gastroenteritis, pathogenesis, Travelers' diarrhea

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## Introduction

### Historical background: the identification of *Escherichia coli* as a digestive pathogen

Many factors contribute to the emergence of infectious diseases. Those frequently identified include microbial adaptation and change, human demographics and behavior, environmental changes, technology, and economic development, breakdown in public health measures and surveillance, and international travel and commerce. To assess the impact of travel on disease emergence, it is necessary to consider the receptivity of geographic zones and their populations to microbial

presentation. Most symptoms do not lead to illness. Life forms that live primarily or entirely within the human body and spread through sexual contact, bead nuclei, and near-physical contact could be transported anywhere in the world in an instant. Where help, tuberculosis, measles, whooping cough, diphtheria, and hepatitis B can be effectively transmitted by travelers and spread to undeveloped geographical areas. In any case, the vaccine-protected population tolerates the condition.

Of all the bacteria, *Escherichia coli* has been studied the most and is the most well-known. German pediatrician Theodor Escherich published the first description of it in

1885. He recognized its significant frequency in the intestinal microbiota of healthy people and its ability to induce illness when directly injected into extraintestinal sites.<sup>1</sup> Unsurprisingly, it took much longer for people to realize that *E. coli* might also cause illness in the gastrointestinal system, which is where it normally lives (for a review, see Robins-Browne).<sup>2</sup>

'Cholera infantum,' a particularly severe type of infantile gastroenteritis that manifested itself in violent outbreaks throughout the early 20th century, was not caused by *E. coli*, despite several claims to the contrary.<sup>2</sup> Reports by Bray and Beavan were crucial factors in the identification of *E. coli* as a main gut pathogen.<sup>3,4</sup> They observed a strong correlation between infantile diarrhea and a specific strain of *E. coli*, which they termed Bacterium coli Neapolitan. Several nosocomial and community outbreaks of *E. coli*-associated diarrhea were documented in the following period, and each epidemic strain was given a distinctive epithet by its discoverer.<sup>2</sup> Fritz Kauffmann, a Danish bacteriologist, cleared up the uncertainty by adapting a serotyping system that he and colleagues had created for *Salmonella enterica* to use with *E. coli*.<sup>5</sup> The foundation of this system is that the surface O (somatic) and H (flagellar) antigens of different *E. coli* isolates may be used to distinguish one strain from another.

The fact that different *E. coli* strains, which had been linked to epidemics of diarrhea in the 1920s and 1940s, belong to a remarkably small number of O serogroups, in particular, O111 and O55.<sup>2</sup> There are now more than 180 O serogroups of *E. coli*, each of which may be further divided into more than 60 H serotypes, creating a total of more than 10000 conceivable combinations. Not all *E. coli* strains, though. Serological type may eventually be replaced by genetic typing, such as multilocus sequence typing, due to these drawbacks as well as the inherent difficulties of standardizing a typing scheme based on antisera generated in various laboratories.<sup>6</sup> In addition to standardizing *E. coli* subtyping, this will also greatly increase its accessibility. Several attempts were made to prove the pathogenicity of these bacteria for animals to prove Koch's postulates in response to the compelling epidemiological data that some *E. coli* strains were causally related to diarrhea. Following the failure of these endeavors (which, as we now know, was caused by the species specificity of these bacteria), researchers began to focus on using humans as their study subjects.<sup>2</sup> The pathogenicity of *E. coli* bacteria from serogroups O111, O55, and O127 for humans was determined by further research. Enteropathogenic *E. coli* (EPEC) is the term used to describe strains of *E. coli* that are primary

intestinal pathogens as opposed to strains whose natural habitat is the intestine and that cause opportunistic infections when introduced into extraintestinal tissues. The term was first used in 1955 by Neter et al.<sup>7</sup>

Several years later, Neter<sup>8</sup> listed the following examples of the data supporting the pathogenicity of EPEC strains: (i) Some strains make volunteers ill with diarrhea; Compared to healthy control participants, EPEC is frequently identified in children with diarrhea; (ii) EPEC are linked to epidemics in institutions; (iii) Some strains make volunteers ill with diarrhea; (iv) Infected individuals with EPEC, both patients and volunteers, produce a particular serological response to the causing bacterium; and (v) The length of the sickness is shortened and outbreaks can be stopped by therapy with drugs that the bacteria are susceptible to. In the years that followed, illnesses with EPEC in industrialized nations decreased in frequency, and curiosity about these bacteria decreased. However, it was discovered in the late 1960s that some strains of *E. coli* can produce dysentery similar to *Shigella* and others can induce diarrhea similar to cholera.<sup>9</sup> This sparked renewed interest in diarrheagenic *E. coli* and gave rise to investigations into their pathogenic characteristics.

#### pathotypes of *E. coli* that cause diarrhea

It is now known that diarrheagenic *E. coli* may be classified into some different pathogenic groups (i.e. pathotypes or biotypes). The clinical, pathological, and epidemiological characteristics of the disease that each pathotype causes are determined by a distinctive collection of virulence-associated variables that interact to form the pathotype (for a comprehensive review, see Nataro and Kaper).<sup>10</sup>

EPEC, enterotoxigenic *E. coli* (ETEC), enteroinvasive *E. coli* (EIEC), enterohemorrhagic *E. coli* (EHEC), and enteroaggregative *E. coli* are the five pathotypes for which Koch's postulates have been confirmed (EAEC; [Table.1](#)). Each pathotype indicates a group of related *E. coli* clones that have gained essential virulence traits through horizontal gene transfer with other bacterial species. The fact that these bacteria belong to different and often non-overlapping O serogroups and O: H serotypes is one indication that they are clonal. The virulence factors specific to each *E. coli* pathotype are different by definition. However, they may be broadly divided into two groups: released toxins, which disrupt the normal physiological functions of host cells, and colonization factors (adhesins), which allow the bacteria to attach tightly to the intestinal mucosa and resist removal by peristalsis.

[Table.2](#) provides an overview of the major virulence factors of the five main pathotypes of diarrheagenic *E.*

*coli*. EPEC and EHEC are the two pathotypes that share virulence determinants. This is likely due to the likelihood that certain EHEC strains originated from EPEC ancestors.<sup>12</sup> However, the majority of the bacteria that Neter and others initially classified as EPEC have shown to be EPEC, as defined presently based on certain virulence determinants<sup>13</sup>.

**Table 1.** Diseases produced by the five main pathotypes of diarrheagenic *Escherichia coli* are characterized by their clinical, pathological, and epidemiological features.

pathotype	Clinical presentation	Intestinal pathology	Susceptible population
ETEC	Watery, cholera-like diarrhea	No notable change	Children in less-developed countries, travelers to those countries
EIEC	Bacillary dysentery	Inflammation and disruption of the mucosa, mostly of the large intestine	All ages, more common in less-developed countries
EPEC	Non-specific gastroenteritis	Attaching effacing lesions throughout the intestine	Children under 2 years of age in less-developed countries
EHEC	Bloody diarrhea	Hemorrhagic colitis, attaching-effacing lesions confined to the large intestine, necrosis in severe cases	Children and the elderly in industrialized countries
EAEC	persistent diarrhea	Inflammation, cytotoxic changes in enterocytes. <sup>11</sup>	Children in less-developed countries, travelers to those countries

**Table 2.** The five main pathotypes of diarrheagenic *Escherichia coli*'s major virulence-associated determinants

pathotype	Adhesins/invasins	Secreted toxins
ETEC	Colonization factor antigens	LT And ST
EIEC	Invasion-plasmid antigens (IpaCetc.)	Sen
EPEC	Fp, intimin	? E-coli-secreted protein F
EHEC	Intimin, ? others	Stx 1 and 2
EAEC	Aggregative adherence fimbriae(AAF/I etc.)	EAST, plasmid-encoded cytotoxin

ETEC, enterotoxigenic *Escherichia coli*. EIEC, enteroinvasive *E.coli*. EPEC, entropathogenic *E.coli*. EHEC, Enterohemorrhagic *E.coli*. EAEC, enteroaggregative *E.coli*. LT, heat-labile enterotoxins. ST, heat-stable enterotoxins, sen, *shigella* enterotoxin. BF, bundle-forming pili. Stx, shiga toxins. EAST, enteroaggregative heat-stable enterotoxin.

## Pathogenic properties of diarrheagenic *Escherichia coli*

### Enterotoxigenic *E. coli*

A useful model for illustrating the concepts underlying the pathogenesis of *E. coli* diarrhea is enterotoxigenic *E. coli*. These bacteria include adhesion molecules, called colonization factor antigens (CFA), that allow them to adhere to the small intestine mucosa, an area where *E. coli* is not often seen in significant quantities. The principal ETEC strains found in humans include a wide range of colonization factors (CFA), including CFA/I, CFA/II, CFA/IV, CFA/III, CS7, and CS17, as well as other putative colonization factors (PCF), such as PCF0148, PCF0159, PCF0166, and PCF8786.<sup>14,15</sup> These colonization elements often take the shape of 2–9 nm-diameter ground fimbriae that bind to certain host cell receptors.<sup>14</sup> Even though the receptors' exact makeup is unknown, many of them most likely exist as oligosaccharide residues on glycoproteins or glycolipids. This conclusion is based on the observation<sup>16</sup> that bacterial adhesion to susceptible cells in vitro can often be blocked by pre-incubating cells with simple sugars. The adhesins of ETEC that infect domestic animals are different from those of human strains because it appears that the interaction between ETEC adhesins and their receptors is host specific.

ETEC release just two types of enterotoxins, known as heat-labile enterotoxin (LT) and heat-stable enterotoxin, in contrast to the various colonization factors they secrete (ST; for a review, see Sears and Kaper).<sup>17</sup> Both physiologically and antigenically, heat-labile enterotoxin and cholera toxin have a tight relationship. Both toxin subunit structures are similar. Consisting of a single A subunit linked to five identical B subunits, the toxin can bind to the Gm1 ganglioside receptor on host cells when they are in their pentameric form. The A1 component of the bound toxin is liberated from the holotoxin and injected into the cytoplasm of the host cell as a result of internalization and processing. It catalyzes the modification of a regulatory subunit of membrane-associated adenylate cyclase, resulting in the latter's irreversible activation. The accumulation of intracytoplasmic CAMP eventually leads to altered electrolyte transport by enterocytes, most notably increased chloride ion secretion by crypt cells and decreased sodium and chloride ion absorption by villous cells. Both of these actions cause luminal electrolyte accumulation, which draws water into the intestine along the resulting osmotic gradient. If the amount of collected intestinal fluid outstrips the large intestine's normal abilities, the surplus is expelled as watery diarrhea, which

characterizes ETEC and *Vibrio cholera* infection. Apart from inhibiting adenylate cyclase activity, cholera toxin and, presumably, LT cause diarrhea by affecting prostaglandin metabolic activity and arousing the enteric nervous system neurotransmitter acetylcholine.<sup>18,19</sup> ST is a low molecular weight peptide having amino acids,<sup>19</sup> in contrast to LT. The intestinal paracrine hormone guanylin, which appears to work by binding to and controlling the activity of membrane-associated guanylate cyclase in small intestine enterocytes, has strong similarities to it.<sup>20</sup> However, guanylate cyclase is irreversibly activated when ST binds to it. This causes an intracellular buildup of cGMP, which has the same function as cAMP, and results in watery diarrhea as a result. The majority of ETEC clinical isolates (around 45%) typically only secrete ST, with ST- and LT-secreting strains being the next most common. Perhaps unexpectedly, given how similar they are to *V. cholera* overall, ETECs that solely produce LT are relatively rare.<sup>15</sup>

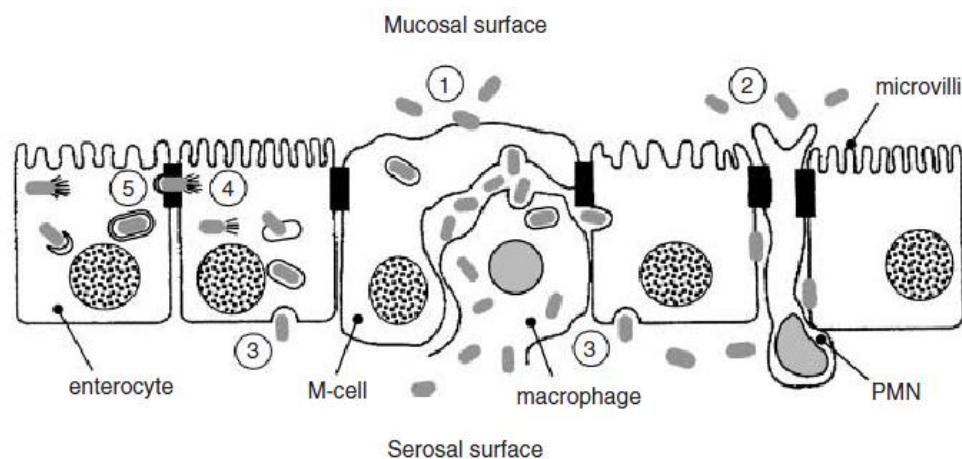
### Enteroinvasive *E. coli*

*Shigella* species, with which they share several essential virulence determinants, are closely related to enteroinvasive *E. coli*. These comprise some genes that are encoded by a large, 220 kb plasmid.<sup>21</sup> Since *Shigella dysenteriae* is the only species of *Shigella* that can produce Shiga toxin, the sickness caused by EIEC is therefore identical to that caused by *Shigella flexneri*, etc., despite being generally less severe (see below). EIEC penetrates the intestinal mucosa, primarily that lining the large intestine, to cause inflammation and mucosal ulceration, which are characteristics of bacillary

dysentery. In contrast to ETEC, which stays within the intestinal lumen throughout infection and does not manifest overt histological damage. Even though *Shigella* and EIEC are models for invasive bacteria, their luminal feature prevents them from penetrating enterocytes. Rather, they pass through M cells, antigen-sampling cells that make up a significant portion of the specialized epithelium that covers the lymphoid follicles in the small and large intestines.<sup>22</sup> By triggering apoptosis in macrophages after penetrating the epithelium, EIEC evades phagocytosis and is subsequently free to enter enterocytes via their basolateral aspect (Figure 1). Although the exact method by which EIEC produce diarrhea is unknown, it may be related to a specific enterotoxin that is encoded by a plasmid.<sup>23</sup>

### Enteropathogenic *E. coli*

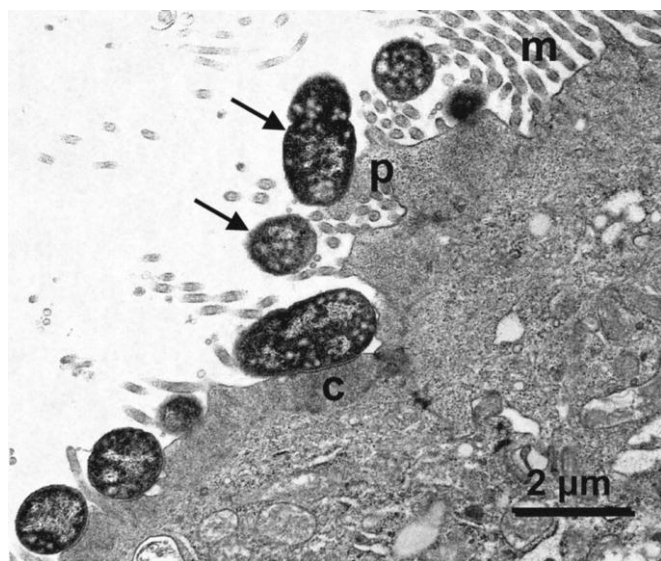
When EPEC first interacts with the intestinal epithelium, it also targets M cells, similar to EIEC. However, unlike EIEC, EPEC stays near the surface of M cells and enterocytes rather than penetrating the epithelium, leading to specific histological alterations known as attaching-effacing lesions (Fig. 2). Unique bundle-forming pili (Bfp),<sup>24</sup> which are encoded by specific plasmids, are believed to be the first point of contact between EPEC and the gut. These pili belong to the type 4 pili family, which also includes the toxin-coregulated pilus of *Vibrio cholera*.<sup>25</sup> Studies on volunteers have shown that Bfp contributes to EPEC's pathogenicity because they experienced a substantially lesser illness than people who ate the wild-type strain.<sup>26</sup>



**Figure 1.** shows a diagrammatic illustration of the stages that enteroinvasive *Escherichia coli* species take to penetrate the intestinal barrier. M cells (1) allow bacteria to enter the intestinal epithelium where they are then discharged into the submucosa. When macrophages undergo bacterial-induced apoptosis, interleukin-1 is released, which sets off an inflammatory cascade that results in tissue damage. In response to early inflammatory signals, polymorphonuclear leukocytes (PMN) are drawn to the infection site. Through tight connections, the PMN moves to the apical side and allows the bacteria access to the intercellular space(2). After passing through one of these two entry points (1 + 2), the bacteria penetrate the enterocytes from the basolateral side(3). Endocytosed bacteria break free from the vacuole and enter the cytoplasm, where they move intracellularly propelled by actin tails (4), spread to neighboring cells via cell junctions (5), lyse the double membrane created by protrusions (6), and then continue their intraepithelial cell-to-cell passage. Incorporated from Sansonetti.<sup>22</sup>

Bfp also has a role in the specific pattern of bacterial adhesion to tissue culture cells. This pattern, known as "localized adherence," offers a practical *in vitro* assay for Bfp presence. Molecular assays, such as a polymerase chain reaction for *bfpA*, the gene for the main structural protein of Bfp, have since supplanted this method. It's interesting to note that other *E. coli* pathotypes, such as EAEC and diffusely adherent *E. coli*, were discovered as a result of using tissue culture cells to test clinical isolates of *E. coli* for the localized adherence phenotype.<sup>27</sup>

A pathogenicity island on the bacterial chromosome houses the bacterial genes necessary to produce the characteristic attaching-effacing lesions linked to EPEC infections. A group of virulence-related genes that are found together on the bacterial chromosome of pathogenic bacteria but missing from non-pathogenic strains of the same species is referred to as a "pathogenicity island." Additionally, pathogenicity islands frequently exhibit signs of bacterial ancestry. The existence of mobile genetic components at their termini and a nucleotide base composition that differs from the chromosome's overall composition are examples of this evidence.



**Figure 2.** Together, these observations suggest showing an electron microscope image of a rabbit's ileum 16 hours after it was inoculated with a strain of enteropathogenic *Escherichia coli* that is particular to rabbits. As shown by pedestal formation (p), accumulation of cytoskeletal proteins (c), and absence of microvilli (m) at sites of bacterial attachment, the attachment-effacement lesions, which include closely connected bacteria (arrows), are accompanied by modifications to the enterocyte cytoskeleton.

Bacterial viruses or plasmids can be used in mechanisms that allow pathogenicity islands to be horizontally transferred across bacteria.<sup>28</sup> Because EPEC requires the pathogenicity island to develop attaching-effacement lesions on enterocytes, it is known as the locus for enterocyte effacement (LEE), which adds to the sticky ability of

EPEC.<sup>29</sup> The non-pathogenic laboratory strain of *E. coli*, *E. coli* K-12, lacks the LEE, but when the LEE is introduced, it endows the strain with attaching-effacing capacity.<sup>30</sup> About 40 genes make up the LEE, which works together to cause attaching-effacement lesions. The type III secretory pathway, a distinctive protein secretory pathway, a group of proteins called *E. coli*-secreted proteins (Esp), which are secreted through this pathway, and the *eae* gene, which codes for the outer membrane protein adhesin intimin, are all encoded by this genes.<sup>31</sup> Type III protein secretory systems are used by many different kinds of harmful bacteria to transfer proteins from the bacterial cytoplasm into the host cell.<sup>32</sup> EspA, a protein encoded by the LEE, is thought to create a tiny hollow tube that joins the bacteria to the host cell in the case of EPEC. EspB and EspD, which are considered to create a pore in the host cell membrane, are two proteins that move via this tube. This pore enables the translocation of additional LEE-encoded proteins like Tir (also known as EspE), which is phosphorylated and functions as an intimin receptor, to the host cell. After Tir binds to intimin, it acts as a location for cytoskeletal protein nucleation, altering cell shape and causing the attaching-effacement lesions to occur. The fluorescent actin staining technique for measuring bacterial attaching-effacement capacity is based on the buildup of cytoskeletal proteins, particularly filamentous actin, at the site of the attached bacteria. In this experiment, bacteria are cultured with tissue culture cells before being reacted with phalloidin that has been fluorescein abelled phalloidin. Using fluorescent microscopy,<sup>33</sup> the latter can be seen because it attaches to filamentous (F-) actin. EspF is a protein that is also encoded by LEE. This is not necessary for the development of attaching-effacement lesions, but it does seem to compromise the integrity of the intestinal epithelium, causing diarrhea.<sup>34</sup> The main secreted protein of EPEC that causes diarrhea may be EspF if there isn't a traditional secreted exotoxin equivalent to LT or ST.<sup>35</sup>

### ***E. coli* enterohemorrhagic**

Two occurrences of hemorrhagic colitis were linked to undercooked hamburger intake in 1982 at a network of American fast-food restaurants.<sup>36</sup> A novel *E. coli* pathotype known as EHEC was discovered as a result of this clinical syndrome, which is characterized by stomach pains, and initial watery diarrhea, followed by bloody diarrhea with little to no fever.<sup>38</sup> In addition to resulting in hemorrhagic colitis, EHEC also causes bloodless, watery diarrhea. It is the primary contributor to the diarrhea-associated hemolytic uremic syndrome in industrialized nations.<sup>39</sup>

EHEC was initially identified from other *E. coli* strains by its serotype, specifically O157: H7, but later it was discovered to produce Shiga toxin (Stx), which has since become the defining characteristic of this pathotype.<sup>40</sup> Verotoxins and Shiga-like toxins are other names for Shiga toxins, which are found in two main antigenic groups: Stx1 (VT-I) and Stx2.<sup>41</sup> Shiga toxin was first discovered in *Shigella dysenteriae*, where it is chromosomally encoded; however, toxin-encoding bacteriophages easily spread the genes for its production between *E. coli* strains. Shiga toxin shares similarities with LT and cholera toxin in its general A1B5 structure. It is internalized by endocytosis through clathrin-coated pits and primarily binds to globotriaosyl ceramide (Gb3) on susceptible host cells. An enzymatically active A1 subunit is then produced after processing by retrograde transport through the Golgi apparatus and endoplasmic reticulum. This compromises the integrity of eukaryotic ribosomes, stopping protein synthesis and causing cell death. Strangely, Stx can partially protect human intestinal epithelial cells from its cytotoxic effects.

The toxin can, however, sneak through the intestinal epithelium and reach the endothelial cells lining the tiny blood veins supplying the kidney, pancreas, heart, and other viscera.<sup>41</sup> The plethora of subsequent metabolic events might result in intravascular coagulation,<sup>42</sup> which would cause thrombocytopenia, microangiopathic hemolytic anemia, erythrocyte fragmentation, and renal failure—the classic triad of HUS.<sup>39</sup> Hemorrhagic colitis and HUS appear to be caused by some but not all strains of *E. coli* that produce Stx. A large plasmid that encodes the unique hemolysin known as enterohemolysin or EHEC hemolysin is often seen in those that do carry virulence factors in addition to Stx, such as the LEE pathogenicity region (which is closely related to that of EPEC). When testing food or clinical samples for the presence of EHEC, diagnostic laboratories can take use of the fact that EHEC can create this hemolysin.<sup>43</sup> Although strains of serotype O157:H7 have been linked to the majority of EHEC-associated diarrhea outbreaks in the Northern hemisphere, including well-publicized outbreaks in the north-western USA,<sup>44</sup> Japan,<sup>45</sup> and Canada,<sup>46</sup> several other serotypes have also been linked to outbreaks and sporadic cases of severe disease.<sup>47</sup> For instance, EHEC of serotype O111: H-<sup>48</sup> was the most prevalent cause of pediatric HUS in Australia over 4 years of national monitoring from July 1994 to June 1998.

**Table 3.** Example of diarrheagenic *Escherichia coli* virulence factors used for the detection and identification of these bacteria in laboratories

Pathotype	Phenotype	Genotype
ETEC	Production of LT or ST	Toxin-encoding genes
EIEC	Invasion of tissue culture cells	Genes located on large invasion plasmid
EPEC	Localized adherence to tissue culture cells, fluorescent actin staining	Genes encoding Bfp, genes located within pathogenicity island
EHEC	Production of Stx, production of EHEC hemolysin, presence of LEE	Genes encoding stx or EHEC hemolysin, genes located within pathogenicity island
EAEC	Aggregative adherence to tissue culture cells	Plasmid-borne encoding adhesive fimbriae or cytotoxin

\*Detectable by polymerase chain reaction or hybridization with a labeled DNA probe. Enterotoxigenic *Escherichia coli* (ETEC), enterotoxigenic *E. coli* (EIEC), enteroinvasive *E. coli* (EIEC), enteropathogenic *E. coli* (EPEC), enterohemorrhagic *E. coli* (EHEC), enteroaggregative *E. coli* (EAEC), the locus for enterocyte effacement (LEE), bundle-forming pili (Bfp), Shiga toxins (Definitions of Diarrhea).

Mild diarrhea was defined as having three to six bowel movements per day with no other symptoms other than mild cramps, which was considered to be diarrhea. Neither of these conditions required confinement to a room or a change in routine daily activities. Mild diarrhea usually involved at least two or three diarrhea movements per day, with cramps, nausea, or both. The diagnosis of moderate diarrhea was made when there were more than four bowel movements per day, along with cramps, nausea, vomiting, and occasionally chills or fever. The severity of these symptoms frequently required confinement to a room for less than a day. More than four bowel movements per day, along with at least four of the following symptoms—nausea, vomiting, cramps, fever, chills, and joint or back pain—constituted severe diarrhea. Some or all of the aforementioned symptoms may also accompany severe diarrhea, necessitating confinement for one or more days.

### Traveler's diarrhea

Traveler's diarrhea is the most common disease that travelers suffer from. Every year, between 20 and 50 percent of passengers on international flights suffer from diarrhea. Symptoms of this disease usually appear in the first week of travel. The most important risk factor is the traveler's destination. Traveling to developing countries such as Latin America, Africa, the Middle East, and Asia increases the chance of contracting this disease. Young adults, people with weakened immune systems, and

patients with diabetes and inflammatory bowel diseases are at higher risk.

Using contaminated water or food is the main cause of infection.

### Summary and conclusions

The identification of these bacteria in the laboratory is now focused on the detection of key virulence markers or virulence-associated phenotypes rather than surrogates, such as serotypes, as a result of the discovery of specific virulence determinants of diarrheagenic *E. coli* (Table 3). The creation of novel vaccines, including ones for ETEC based on colonization factor antigens or LT toxoids, has also been sparked by a better knowledge of virulence.<sup>49,50</sup>

Piglets, sheep, and cattle with enterotoxigenic *E. coli* infections suffer from serious economic problems. Vaccines containing adhesion proteins made from ETEC or bacteria that have been genetically modified to express these proteins can help to regulate them to some extent.<sup>51</sup>

The vaccine is typically given to pregnant animals, who then pass on protective immunity to their young through colostrum.<sup>51</sup> For human infections with ETEC, both active and passive immunization—the latter utilizing hyperimmune cow colostrum—are being considered.<sup>52,53</sup>

It does not bode well for ETEC vaccines based on these methods, nevertheless, given the high number of antigenically different CFA of human ETEC strains and rising evidence that more such factors remain to be identified.<sup>54</sup> Oral rehydration with sugar- and electrolyte-containing liquids is the cornerstone of antidiarrheal therapy.<sup>55</sup> Understanding the underlying causes of the fluid and electrolyte transport abnormalities that result from infectious diarrhea is necessary for this. Additionally, research is being done on treatment options for EHEC infection using inert ligands or even genetically modified strains of *E. coli* bacteria that adsorb Stx in the gut lumen before the toxins enter the body.<sup>56,57</sup>

It's crucial to note that patients who are thought to have these bacteria in their bodies shouldn't receive antibiotic treatment. Antibiotics may increase the production of toxins or encourage their release from the bacteria, which increases the risk of hemorrhagic colitis or HUS.<sup>58</sup> Last but not least, research into the virulence of *E. coli* has uncovered fascinating new details about the development and evolution of bacterial pathogens in general. For instance, a comparison of the genomic sequences of *E. coli* K-12, a healthy laboratory strain, and EHEC O157:H7 has shown that these bacteria share a DNA backbone that contains numerous islands of DNA that were acquired over an extended period by the integration of plasmids, transposons, and bacteriophages.<sup>59</sup> New pathotypes of *E. coli* will continue

to develop in the future due to *E. coli's* continuing stepwise development, which enables it to adapt to constantly changing circumstances and surroundings.

### Review Highlights

#### What does *E. coli* diarrhea look like?

watery diarrhea lasts for about a day and then may change to bright red bloody stools. The infection makes sores in your intestines, so the stools become bloody. Bloody diarrhea may last for 2 to 5 days. You might have 10 or more bowel movements a day.

#### What type of diarrhea does *E. coli* cause?

Depending on the virulence factors they possess, virulent *Escherichia coli* strains cause either noninflammatory diarrhea (watery diarrhea) or inflammatory diarrhea (dysentery with stools usually containing blood, mucus, and leukocytes).

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### Conflict of Interest

The authors have no conflict of interest to declare.

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