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# Emerging Role of Enterohemorrhagic *Escherichia Coli* As a Global Foodborne Pathogen

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## Abstract

Enterohemorrhagic *Escherichia coli* (EHEC) constitute a subgroup of serotypes (*E. coli* O157 and some other serogroups) of Shiga toxin producing *E. coli* (STEC) that is associated with severe human diseases like bloody diarrhoea and haemolyticuraemic syndrome. EHEC is an important global zoonotic foodborne pathogen, which is reported from developing as well as developed nations of the world. EHEC rarely causes disease in animals but ruminants are recognized as their main natural reservoir. Cattle are considered to be the most important source of human infections with EHEC O157. Faecal-oral- route is the chief mode of transmission. Humans may acquire infection by the ingestion of raw ground beef, other animal products and contaminated fruits and vegetables, direct contact with animal carriers, their faeces, and contaminated soil or water. The affected persons exhibit the signs of water diarrhea, hemorrhagic colits, abdominal tenderness, severe abdominal cramps, low grade fever, nausea, vomiting, dehydration, hemolytic anemia, and kidney failure. The mainstay of treatment is the assessment of dehydration and replacement of fluid and electrolytes. Proper hand washing after using the lavatory or changing a diaper, especially among children or those with diarrhea is imperative to reduce the risk of transmission.

**Keywords**: *Escherichia coli*, Enterohemorrhagic, Foodborne infection, Public health, Zoonotic pathogen

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## 1. INTRODUCTION

*Escherichia coli,* a Gram-negative, facultative anaerobic, rod-shaped, coliform bacterium of the genus *Escherichia*, is commonly found in the lower intestine of warm-blooded organisms [1, 2]. The commensal relationship between the bacterium and its host is symbiotic, providing both with a number of advantages. However, *E. coli* has developed into a pathogen well adapted to its host through the loss and gain of genes. Some pathogenic *E. coli* strains cause diarrheal illness (intra-intestinal pathogenic *E. coli*), whereas others cause extra-intestinal infections (extra-intestinal pathogenic *E. coli* [3].Pathogenic *E. coli* can be released with the wastes coming from slaughterhouses into the environment, where they can persist. Nevertheless, some strains have evolved the capability to cause both intestinal and extra-intestinal illnesses. The different pathogenic *E. coli* are characterized by particular subsets of genes associated with the virulence, identifying distinct groups or pathogroups [4, 5].

Most *E. coli* strains are harmless, but some serotypes can cause serious food poisoning in their hosts, and are occasionally responsible for food contamination incidents that prompt product recalls [6]. The harmless strains are part of the normal microbiota of the gut, and can benefit their hosts by producing vitamin K2, (which helps blood to clot) and preventing colonization of the intestine with pathogenic bacteria, having a symbiotic relationship [7]. Although the majority of *E. coli* strains are harmless, certain strains are pathogenic and cause diseases, such as watery diarrhea, bloody diarrhea, urinary tract infection, meningitis, and sepsis, which can lead to death [8]. The organism is expelled into the environment within fecal matter. The bacterium grows massively in fresh faecal matter under aerobic conditions for three days, but its numbers decline slowly afterwards [9].

*Escherichia coli* can be grown and cultured easily and inexpensively in a laboratory setting, and has been intensively investigated for over 60 years. The organism is a chemoheterotroph whose chemically defined medium must include a source of carbon and energy [10].*Escherichia. coli* is the most widely studied prokaryotic model organism, and an important species in the fields of biotechnology and microbiology, where it has served as the host organism for the majority of work with recombinant DNA. Under favorable conditions, it takes as little as 20 minutes to reproduce [11].

Enterohemorrhagic *Escherichia coli* (EHEC), a subset of pathogenic *E. coli,* can cause diarrhea or hemorrhagic colitis in humans [12]. The infection with this type of pathogenic bacteria may lead to hemorrhagic diarrhea, and also kidney failure; these have been reported to cause the deaths of children younger than five years of age, of elderly patients, and of patients whose immune systems are otherwise compromised. Hemorrhagic colitis occasionally progresses to hemolytic uremic syndrome (HUS), an important cause of acute renal failure in children and morbidity and mortality in adults. Enterohemorrhagic *E. coli* O157:H7 (EHEC O157:H7) has been known to cause these syndromes since the 1980s, but clinical cases and outbreaks caused by members of other EHEC serogroups are increasingly recognized [13]. What all of the HUS-associated *E. coli* seem to have in common is the ability to produce verotoxins, together with the ability to bind to and colonize human intestines. Because verotoxin genes can be transmitted between bacteria, additional *E. coli* pathotypes associated with HUS could also be discovered [14, 15].

The most known strain of pathogenic *E. coli* is the EHEC strain. EHEC serotype O157:H7 is well known as the causative agent of outbreaks of food-associated severe diarrhea. Infection with O157:H7 results in severe abdominal cramps and bloody diarrhea and may lead to hemolytic-uremic syndrome (HUS) which can be life-threatening [16]. The most common foods associated with transmission of these bacteria are undercooked meat (especially ground beef), raw milk, and raw vegetables. Enterohemorrhagic *Escherichia coli* strains do not directly invade the enterocytes, but produce toxins that do enter and severely damage these cells. The responsible cytotoxins are verotoxins I and II (designated as Shiga toxins, Stx-1 and Stx-2). The Shiga toxins are capable of inactivating ribosomes, blocking protein synthesis, and emerging through the basolateral membrane into the sub-epithelial region.

Stx-2 is seen most often in the EHEC strains that cause HUS [3, 16, 17].

Ruminants, particularly cattle and sheep, seem to be the maintenance hosts for EHEC O157:H7 and many other verotoxin-producing *E. coli.* Some, but not all, individual animals carry these organisms in the intestinal tract, and shed them in the feces. Members of other animal species are also infected occasionally [11, 18]. Most infected animals do not develop any clinical signs, although members of some non-O157 serogroups may cause enteric disease in young animals, and EHEC O153 has been linked to a disease that resembles HUS in rabbits [19, 20]. Humans acquire EHEC by direct contact with animal carriers, their feces, infected people, and contaminated soil or water, or via the ingestion of underdone meat, other animal products, contaminated vegetables and fruit, and other foods [21]. The infectious dose for people is very low, which increases the risk of disease. Animals do not seem to be reservoirs for enteroaggregative, verotoxin-producing *E. coli*, which are probably maintained in humans, but can also be acquired in food [22].

## 2. EPIDEMIOLOGY – PUBLIC HEALTH IMPACTS

*Escherichia coli* are widely distribution as evidenced by the isolation from many countries of the world. The route of infection is fecal-oral, predominantly via contaminated water and food. The source of *E. coli* and other gram-negative bacterial pathogens in neonatal infections is often through the maternal genital tract. Hospital acquisition of gram-negative organisms through person-to-person transmission from nursery personnel or environmental sites can occur. The incubation period is variable with time of onset of infection ranging from birth to several weeks after birth [21, 23].

Enteric *E. coli* are part of the natural flora of many animals. Human infections occur through consumption of contaminated food products (undercooked meat, or contaminated fresh produce such as salad leaves), drinking water contaminated with animal or human waste, or through direct person-to-person spread from poor hygiene. Enterohemorrhagic *Escherichia coli* (EHEC) and more recently EAEC and STEAEC are the main *E. coli* pathotypes associated with food poisoning outbreaks in the developed world [24].

### 1.2. Virulence Factor and Pathogenesis

The processes by which epithelia are infected by pathogenic *E. coli* start by the attachment of bacteria to specific host cells. To do this, pathogenic bacteria express a wide variety of surface-exposed adhesions responsible for specific binding to structural or functional cell membrane-associated molecules [25]. The attachments onto the target host cells allow enteric and urinary tract bacterial pathogens to resist clearance by peristalsis and micturition, respectively. The bacterial adhesion to target host cells can be more than a simple attachment due to pathogen-specific recognition of host cell membrane-associated molecules, since several of these molecules functioned intrinsically as signaling molecules or after recognition/ activation recruited cytosolic signaling molecules [14, 18, 21].

Attachment by fimbrial or afimbrial structures allows bacterial pathogens to interact with the host cell membrane to ensure the optimal delivery of their cytotonic or cytotoxic toxins in the vicinity of their membrane-associated receptors, triggering signaling events that affect transport/secretion functions or the cell structural organization. For other pathogenic bacteria, adhesive factors allow the intimate association of bacteria with the cell membrane that is necessary for the initiation and completion of signaling controlled structural lesions, which in turn dramatically impair host cell functions [26]. For invasive bacterial pathogens, attachment initiates an orderly series of signaling-controlled events that lead to host cell membrane rearrangements that are necessary for the achievement of bacterial cell entry followed by the development of sophisticated bacterial intracellular lifestyles.

Two major classes of adhesins are present on the bacterial sur-face of Gram-negative pathogens: the fimbrial adhesins, consisting of linear homopolymers or heteropolymers, and the afimbrial adhesins, formed of single proteins or homotrimers[27].The biogenesis of flagella involves the coordinated structural assembly of flagellar proteins. Afa/Dr DAEC strains

are heterogeneous in terms of hemolysin expression, suggesting a variable distribution of the part of PAICFT073 containing the *hly*gene among the Afa/Dr DAEC strains [28].

The virulence factors of pathogenic strains of *E. coli* include capsules, endotoxin, structures responsible for adherence and colonization, enterotoxins and other secreted substances.Capsular polysaccharides, which are produced by some *E. coli* strains, interfere with the phagocytic uptake of these organisms. Capsular material, which is weakly antigenic, also interferes with the antibacterial effectiveness of the complement system [8, 12, 15]. Endotoxin, a lipopolysaccharide (LPS) component of the cell wall of Gram-negative organisms, is released on death of the bacteria. It is composed of a lipid A moiety, core polysaccharide and specific side chains. The role of LPS in disease production includes pyrogenic activity, endothelial damage leading to disseminated intravascular coagulation, and endotoxic shock. These effects are of greatest significance in septicaemic disease [24, 29].

Fimbrial adhesins, which are present on many strains of *E. coli* allow attachment to mucosal surfaces in the small intestine and in the lower urinary tract. Firm attachment to the mucosa facilitates colonization by diminishing the expulsive effects of peristalsis and the flushing effect of urine. The most significant adhesins in strains of *E. coli* producing disease in domestic animals are K88 (F4), K99 (F5), 987P (F6), F18 and F41. The more recent system of nomenclature uses ‘F’ and a number to identify particular fimbriae. The reason for the ‘K’ used under the older system is because originally some of the fimbrial adhesins were mistakenly thought to be capsular (K) antigens. The use of ‘P’ derives from the term pilus, because fimbriae are sometimes known as pili [18, 22, 30].

The most common adhesin present in strains of *E. coli* infecting pigs is K88. The receptor for the K88 antigen is encoded by a dominant gene and thus if a sow is homozygous recessive for the gene, her colostrum contains no anti-K88 antibody, resulting in highly susceptible piglets. F41 adhesins occur in calves and K99 in calves and lambs. Although the numbers of receptors for K88 adhesins on pig enterocytes decline with age, K88+*E. coli* strains may cause diarrhoea in piglets after weaning. Receptors for F18 are found only in older piglets and thus F18+ strains are important in post-weaning diarrhoea and oedema disease. Although neonatal piglets are susceptible to strains of *E. coli* bearing F6 adhesins, resistance to colonization develops by 3 weeks of age. Both K88 and K99 adhesins are encoded by plasmids [15, 31].

The pathological effects of infection with pathogenic *E. coli*, other than those attributed to endotoxin, derive mainly from the production ofenterotoxins, shigatoxins or verotoxins or cytotoxic necrotizing factors. Unlike enterotoxins which affect only the functional activity of enterocytes, shigatoxins and cytotoxic necrotizing factors can produce demonstrable cell damage at their sites of action [28, 30].

### 2.1. Transmission and Clinical Signs

Enterohemorrhagic *Escherichia coli* (EHEC) are transmitted by the fecal–oral route. EHEC can spread between animals by direct contact or via water troughs, shared feed, contaminated pastures or other environmental sources. Birds and flies are potential vectors. In one experiment, EHEC O157:H7 was transmitted in aerosols when the distance between pigs was at least 10 feet. The organism was thought to have become aerosolized during high pressure washing of pens, but normal feeding and rooting behavior may have also contributed [26, 30].

People mainly become infected with EHEC O157:H7 by ingesting contaminated food and water, or during contact with animals, faeces and contaminated soil. The infectious dose for humans is estimated to be less than 100 organisms, and might be as few as 10. Foodborne outbreaks caused by EHEC O157:H7 are often associated with undercooked or unpasteurized animal products, particularly ground beef, but also other meats and sausages and unpasteurized milk and cheese. Additional outbreaks have been linked to lettuce, spinach, various sprouts and other contaminated vegetables, unpasteurized cider, nuts and even pickled vegetables [15, 17, 18]. Contaminated irrigation water is an important source of EHEC O157:H7 on vegetables. This organism can attach to a variety of edible plant material, although it seems to

bind more readily to some fruits and vegetables than others. Cattle transmit EHEC to humans by shedding the pathogen in their feces. Fecal shedding may be brief or more extended [23].

Infection with *E. coli* O157:H7 can occur from ingestion of the contaminated food or water, or oral contact with contaminated surfaces. Examples of this can be undercooked ground beef but also leafy vegetables and raw milk. Fields often get contaminated with the bacterium through irrigation processes or contaminated water naturally entering the soil. It is highly virulent, with a low infectious dose: an inoculation of fewer than 10 to 100 CFU of *E. coli* O157:H7 is sufficient to cause infection, compared to over one-million CFU for other pathogenic *E. coli* strains [22, 26].

The incubation period of disease is 1 to 6 days. Most infections become apparent after 3-4 days. The affected persons exhibit the signs of water diarrhea, hemorrhagic colits, abdominal tenderness, severe abdominal cramps, low grade fever, nausea, vomiting, dehydration, hemolytic anemia and kidney failure. Other sings include irritability, lethargies, seizures, paresis, stroke, cerebral oedema, pleural effusion, and respiratory distress. The infection is severe in children, elderly, pregnant women and immune compromised persons [32].

*Escherichia coli* O157:H7 infection often causes severe, acute hemorrhagic diarrhea (although nonhemorrhagic diarrhea is also possible), and abdominal cramps. Usually little or no fever is present, and the illness resolves in 5 to 10 days [17, 18]. It can also sometimes be asymptomatic. In some people, particularly children under five years of age, persons whose immunologies are otherwise compromised, and the elderly, the infection can cause hemolytic uremic syndrome (HUS), in which the red blood cells are destroyed and the kidneys fail. About 2–7% of infections lead to this complication. In the United States, HUS is the principal cause of acute kidney failure in children, and most cases of HUS are caused by E. coli O157:H7 [33, 34].

## 3. DIAGNOSIS AND PUBLIC HEALTH IMPORTANCE

The isolation of the pathogen from food or stool specimens involves first enrichment in a selective broth and then plating on to cefiximetellurite sorbitol McConkey agar (CT-SMAC). On this medium, slightly transparent, almost colourless colonies with a week pale brownish appearance having a diameter of 1 mm [9, 14]. Such presumptive colonies should be subcultured on to nutrient agar for biochemical tests. Other methods such as multilocus enzyme electrophoresis, plasmid profile analysis, pulse field gel electrophoresis may further differentiate the organism. PCR can be used to detect the bacteria in environmental samples. Direct immunolureseence (DIF) is helpful to demonstrate the pathogen in human faeces [15, 18, 32].

A stool culture can detect the bacterium, although it is not a routine test and so must be specifically requested. The sample is cultured on sorbitol-MacConkey (SMAC) agar, or the variant cefixime potassium tellurite sorbitol-MacConkey agar [35]. On SMAC agar, O157:H7 colonies appear clear due to their inability to ferment sorbitol, while the colonies of the usual sorbitol-fermenting serotypes of E. coli appear red. Sorbitol non-fermenting colonies are tested for the somatic O157 antigen before being confirmed as E. coli O157:H7. Like all cultures, diagnosis is time-consuming with this method; swifter diagnosis is possible using quick E. coli DNA extraction method, plus PCR techniques. Newer technologies using fluorescent and antibody detection are also under development [36].

Earlier, the avian strains of *E. coli* were considered as not causing any important disease in humans and animals, so were not of much zoonotic significance. But as APEC share not only identical serotypes but specific virulence factors also with human pathogens, their zoonotic potential is now under consideration and is not under a single platform. However, colibacillosis is considered as food or water-borne zoonotic disease transmitted to humans via the fecal-oral route. In this context, Pal [37] has listed many avian diseases of

multiple etiologies that are transmitted to humans involving several routes. Among these zoonotic infections, colibacillosisis and salmonellosis are the leading cause of human illness [5]. Resistant strains from the gut readily soil the poultry carcasses at slaughter, and as a result, poultry meats are often contaminated with multi-resistant *E. coli*. In a similar fashion, the eggs become contaminated during laying time.

### 3.1. Treatment - Control and Prevention

The mainstay of treatment is the assessment of dehydration and replacement of fluid and electrolytes. While fluid replacement and blood pressure support may be necessary to prevent death from dehydration, most patients recover without treatment in 5-10 days. There is no evidence that antibiotics improve the course of disease, and treatment with antibiotics may precipitate hemolytic uremic syndrome.

The antibiotics are thought to trigger prophage induction, and the prophages released by the dying bacteria infect other susceptible bacteria, converting them into toxin-producing forms. Anti-diarrheal agents, such as loperamide (imodium), should also be avoided as they may prolong the duration of the infection [38, 39, 40].

*Escherichia coli* are bacteria found in the environment, foods, and intestines of people and animals. Most *E. coli* are harmless and are actually an important part of a healthy human intestinal tract. However, some *E. coli* can cause diarrhea, urinary tract infections, respiratory illness, bloodstream infections, and other illnesses. The types of *E. coli* that can cause illness in humans are mainly can be transmitted through contaminated food or water [37,41].

Proper hand washing after using the lavatory or changing a diaper, especially among children or those with diarrhea, reduces the risk of transmission. Anyone with a diarrheal illness should avoid swimming in public pools or lakes, sharing baths with others, and preparing food for others and even avoiding raw milk [41,42, 43]. Good management practices designed to minimize the exposure level of the organisms in the bird's environment are necessary in any preventive program. It is essential to avoid overcrowding and provide proper ventilation along with good bio-security measures and appropriate sanitation and hygiene standards at the poultry farms to control of colibacillosis in birds, and thereby, reducing its zoonotic incidences [41, 44].

In addition, efficient treatment, control and prevention measures are necessary as they are described in figure 1 for food security, food protection, environmental sanitation, personal cleanliness, through cooking of food before consumption, and health education of food handlers, housewives and persons engaged in food establishment about the source of infection, severity of disease and importance of personal hygiene are highly imperative to minimize the incidence of disease in humans [37,41,45,46,47,48].

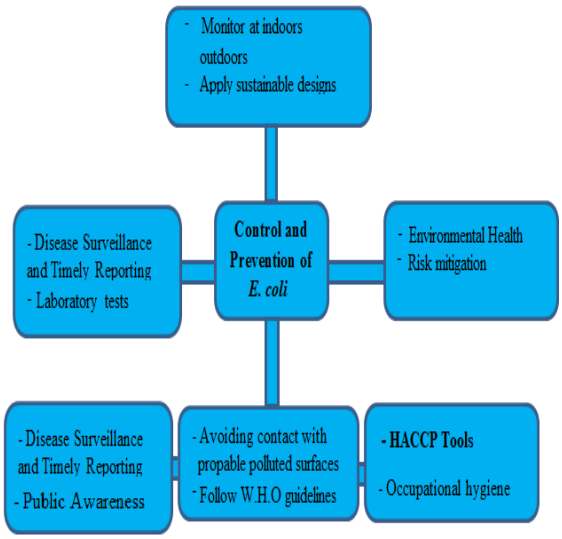


**Figure 1.** Prevention measures to be taken for the food security and control of *E. coli*.

However, in figure 1 are presented necessary measures that could be taken for public health protection in relation to proper application of sustainable designs, utilities so as to mitigate associated risks. Disease surveillance is necessary for qualitattive environmental health conditions at indoor,

oudoor environments promoting proper use of sustainable green designs protecting public health so as to protect public health and to mitigate associated health risks at post pandemic covid-19 era [45,46,47,48].

## 4. CONCLUSIONS

Enterohemorrhagic *Escherichia coli* (EHEC), a bacterial pathogen, which is responsible for outbreaks of bloody diarrhea and hemolytic uremic syndrome is prevalent globally. The pathogen can spread between animals by direct contact or via water troughs, shared feed, contaminated pastures or other environmental sources. Birds and flies are potential vectors. *Escherichia coli coli* O157:H7 infection often causes severe, acute hemorrhagic diarrhea (although nonhemorrhagic diarrhea is also possible), and abdominal cramps.

The pathogen has great a zoonotic significance as reported from many countries of the world. Good management and proper sanitation reduce the chance of occurrence and spread of the pathogen. As poultry meat is considered an important cause of human food poisoning, it is emphasized that meat must be thoroughly cooked before consumption. Further attempts should be made for eliminating colibacillosis from the poultry flocks, in order to prevent potential hazards to the public health.

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## CONFLICT OF INTEREST

The authors declare that they do not have conflict of interest.

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