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Pathogenesis of *Escherichia coli*: A Clinical Findings

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Authors' contributions

This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.

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Review Article

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ABSTRACT

Theodore Escherich, a German doctor, found *E. coli* for the first time while studying the gut flora of newborns. Bacterium coli commune (Escherich 1885) was named after him in 1885, and its virulence in extraintestinal illnesses was established by him (1894 Escherich). Until 1919 the term Bacterium coli was commonly used. Then after the formation of the genus Peschiera, Castellani and Chalmers called the type species *E. coli* (Chalmers & Castellani 1919).

Escherichia coli is a member of the Enterobacteriaceae family and is a gram-negative facultatively anaerobic rod (with both a fermentative and respiratory metabolism) that lacks oxidase production. One single rod cell of *Escherichia coli* cell is generally 1.1–1.5 m broad by 2–6 m long. They may be motile or nonmotile, producing lateral flagella instead of polar flagella when motile. Many strains expand fimbriae or pili, which might be proteinaceous appendages (or structures or fibers) that extend outwardly from the bacterial cell and assist in bacterial mobile adhesion or adherence to other host cells or tissues.

Shigella spp. are closely related to *Escherichia coli*, albeit Shigella is less biochemically active than most *E. coli* strains. Although genetic relatedness allows Shigella and *E. coli* to be classified as a single genus, the two have typically been kept apart to avoid medical diagnostic confusion.

E. coli are found in many living organisms' nature, edibles, water, and intestines. *E. coli* is a giant

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and numerous organization. Most *E. coli* traces are secure; some can purpose the contamination. Some *E. coli* strains are chargeable for causing diarrhea, and lots of other lines motive urinary tract infections, pneumonia, and lots of different infections and diseases.

Keywords: E. coli; microbiology; metabolic; organism; prokaryotic; eukaryotic; diarrhea.

1. INTRODUCTION

In the stomachs of homo sapiens and creatures with warmblood characteristics, *Escherichia coli* (*E. coli*) is standard. The broad majority of *E. coli* strains are entirely safe to consume. Few, such as Shiga toxin-producing *E. coli* (STEC), can, nevertheless, cause significant foodborne illness. Humans become infected by consuming tainted foods such as uncooked ground beef, unpasteurized milk, and tainted fresh vegetables and sprouts.

Microorganisms that oxidase-terrible, gram-terrible, rod-fashioned, motile through peritrichous flagella and non-spore generating belong to this genus. They are anaerobic, which means they produce fuel from complex sugars. These are methyl red high-quality and Voges–Proskauer poor. Several lines create polysaccharide drugs or microcapsules. These are o-nitrophenyl-b-D-galactopyranoside superb & those generate indole, are unable to hydrolyze urea, and are incapable of growing in Miller's KCN broth. No hydrogen disulfide is formed, phenylalanine isn't deaminated, gelatin isn't liquefied, and gluconate is not oxidized on triple sugar iron (TSI) or Kligler's iron agar (KIA). Although most bacteria decarboxylate lysine and utilize sodium acetate, Simmons' citrate agar does not support their growth. Other Escherichia species include Escherichia blattae, Escherichia fergusonii, Escherichia hermannii, and Escherichia vulneris. The sixth species is Escherichia albertii [1].

2. PATHOGENIC *Escherichia coli*

E. coli strains can cause septicemia, pneumonia, meningitis, bladder and kidney infections, hemolytic–uremic syndrome (HUS), diarrhea, and dysentery, to name a few. On the other hand, different strains with diverse virulence genes cause varied signs and symptoms. Despite their diverse toxicity, the vast species of *E. coli* strains found in the colon must be classified as non-virulent.

Various highly adaptive *E. coli* clones have begun showing unique virulence characteristics, allowing them to survive in novel surroundings and leading to a vast spectrum of illnesses. These virulence features are usually stored on genetic elements that may be used to create new virulence factor combinations in new strains or genetic elements that were formerly mobile but have since evolved to be 'locked' into the genome. The combinations of most potent virulence factors only have lived past to be called unique *E. coli* 'PATHOTYPES' allowing them to affect healthy individuals. Enteric/diarrhea, urinary tract infections (UTIs), and sepsis/meningitis are the three most common illnesses. The six forms of intestinal pathogens include enteropathogenic *E. coli* (EPEC), enterohaemorrhagic *E. coli* (EHEC), enterotoxigenic *E. coli* (ETEC), enteroaggregative *E. coli* (EAEC), enteroinvasive *E. coli* (EIEC), and diffusely adherent *E. coli* (DAEEC). Uropathogenic *E. coli* causes UTIs, the most common *E. coli* infections outside of the gut (UPEC). Meningitis-associated *E. coli*, the serotype that leads to meningitis and sepsis, is proving to be an increasingly prevalent source of extra enteric disorders (MNEC). *E. coli* pathotypes linked to extraintestinal infections are now known as ExPEC. EPEC, EHEC, and ETEC all employ many of the same pathogens to produce sickness in animals [2].

3. VIRULENCE FACTORS

In E Coli, two types of virulence factors have been recognized: toxins & surface antigens.

4. SURFACE ANTIGENS

• **Antigen**: Endotoxin activity is caused by the somatic lipopolysaccharide O antigen. The protection of the organism against phagocytosis and bactericidal actions is mediated by complement. Standard serum envelope or K antigens defend against phagocytosis and antibacterial agents. Antibodies to the K & O antigens stop these activities from happening. The Kl envelope antigen is carried by the *E. coli* that causes septicemia & infant meningitis; the group B antigen of meningococci is comparable.

In early attachment and colonization crucial role is played by Fimbriae.

Due to the discovery of Colonisation factor antigens (CFA) in the enterotoxigenic, Escherichia is the cause of diarrhea in males & females. Fimbriae are also required for the organism's adherence during a urinary tract infection [2].

As shown in uropathogenic strains, human erythrocytes and uroepithelial cells have P blood group material that binds solely to P fimbria.

Toxins: *E. coli* develops two types of exotoxins: enterotoxins & hemolysins

• even though virulent strains manufacture them more frequently than avirulent strains, a function in pathogenesis is not seen to be played by hemolysis.

• In uropathogenic *E. coli*, CNF I (cytotoxic necrotizing factor-1) and siderophores are essential components of adhesion & biofilm formation. • In the development of diarrhea, Enterotoxins are involved. *E. coli* enterotoxins detected are of three types, (ST) heat-stable toxin, (VT) verotoxin & heat (LT)labile toxin, which is together given the terminology " Shiga-like toxin (SLT)."

• *E. coli* LT (heat-labile toxin) (De and colleagues found it in samples from adult diarrhea patients in Calcutta in 1956). Antigenic features, structure & mode of action, *E. coli* is comparable to cholera toxin [3]. Each unit consists of a polypeptide subunit complex with five B subunits (B for binding) & one active subunit A. Subunit B of the toxin binds to the GMT ganglioside receptor present on the epithelial cells of the intestine, causing subunit A to divide into two fragments, Al & A2. The Al fragment leads to the activation of the adenyl cyclase present in the enterocytes, producing cyclic adenosine 5' monophosphate (cAMP), which increases water and electrolyte outflow into the bloodstream [3].

The heat-stable toxin (ST) of *E. coli* was discovered in 1970 and is composed of antigenic polypeptides with a low molecular weight. STB and STA (or ST I, which is methanol soluble) are two ST (or ST-II, insoluble in methanol) forms [4].

In the stomach, STA activates cyclic guanosine monophosphate (cGMP). Within the duration of intragastric treatment of four hours, it causes fluid buildup in the intestines of newborn mice. A baby mouse is a frequent tool for demonstrating STA [4].

ST B causes fluid accumulation in young piglets (age: up to about nine weeks), but this is not seen in the baby mice. Although there is uncertainty in the mechanism of action, it excludes cAMP or cGMP. ST genes can be found on plasmids with other genes such as drug resistance genes and LT genes. On the other hand, the genes STA & STB are not identical plasmids [4].

• Verocytotoxin, commonly termed verotoxin, is a cytotoxic substance produced by *E. coli* that affects the Vero cells (i.e., the cell line created from Afrin green monkey's kidney cells). Because of its physical, antigenic, and biological similarities to Shigella dysenteriae type 1 toxin, it's also recognized as a Shiga-like toxin (SLT). It acts by the inhibition of the creation of proteins. VT, like Shiga toxin, causes enterotoxicity in rabbit ileal loops and produces toxicity in Vero and HeLa cells. Both A and B subunits are present in VT. The genes in question are seen to be phage-encoded. VT 2 has been discovered as an antigenically different VT that does not neutralize it, unlike VT 1 and Shiga, antitoxin [5].

5. CLINICAL INFECTIONS CAUSED

E. coli gives rise to four distinct types of infections in the host:

- Urinary tract infection
- Diarrhea
- Septicemia, neonatal sepsis & neonatal meningitis
- Pyogenic infections [5].

The great majority of spontaneously acquired urinary tract infections are caused by *E. coli* and other coliforms (UTI). *E. coli* serotypes that are typically prevalent in a person's gut, such as O groups 1, 2, 4, 6, 7, and so on, cause community-acquired UTI (Case 1). Bacteria such as Pseudomonas and Proteus are more common in samples acquired following hospital instrumentation [6].

Infection can be induced by urinary obstruction caused by prostatic hypertrophy, calculi, or pregnancy. Asymptomatic bacteriuria has been reported in 5-7 percent of pregnant women, which, if left untreated, can lead to infections that will appear with diverse symptoms later in pregnancy, pyelonephritis & hypertension [6].

While 'ascending infections' induced by gut flora can cause lower urinary tract infections,

pyelonephritis is most commonly caused by hematogenous spread. Most cystitis isolates lack K antigens, but bacteria that express K antigens are more likely to cause pyelonephritis. In general, *E. coli* that are P pili positive are uropathogenic [6].

6. ADHESION/COLONIZATION

Adhesion factors in pathogenic *E. coli* strains lead to the colonization of the bacteria where it doesn't usually survive, for example, the jejunum, duodenum ileum, and the urethra. The most simple morphological structures created by adhesins are fimbriae (also called pili) or fibrillae, classified into various categories. Fimbriae are non-flagella rod-like structures having a diameter of 5–10 nm. Fibrillae can be long and wiry or curly & springy, with a 2–4 nm diameter. Afa adhesins, which are described as fimbrial adhesins but appear to contain a thin fibrillar part that is not so easy to visualize, are formed by several diarrhoeagenic and uropathogenic *E. coli* strains. Supramolecular proteins, outer-membrane proteins. If the bacteria comes into touch with the correct receptor, even surface characteristics on commensal *E. coli* strains can trigger signaling cascades. TLR4 binds to *E. coli* LPS and other Gram-negative bacteria's LPS, initiating a solid cytokine cascade that can initiate septic shock and death. Flagellin, the main component of flagella, can bind to TLR5, causing interleukin-8 production and an inflammatory reaction [7].

7. PATHOTYPES AND PATHOGENESIS/ DIARRHEAGENIC *E. coli*

- Enteropathogenic *E. coli*
- Enterotoxigenic *E. coli*
- Enteroinvasive *E. coli*
- Enterohemorrhagic *E. coli*
- Enteroaggregative *E. coli*
- Diffusely adherent *E. coli* **(DAEC)** [8]

EPEC: These bacteria have been related to diarrhea in babies and children, mainly due to institutional outbreaks, but they can also cause sporadic diarrhea in children and adults.

The presence of O antigens distinguishes EPEC. Colonies produced on cultivating with polyvalent & monovalent EPEC-O antisera can be detected via slide agglutination. EPEC is neither invasive nor creates enterotoxins. The plasmid-encoded protein EPEC adherence factor (EAF) has been related to attachment in infantile enteritis. One more approach is adhesion to the enterocyte membrane. Such action is controlled by the chromosomally coded enterocyte effacement locus (L) [8].

Diarrhea induced by **enterotoxigenic *E. coli* (ETEC)** falls into two categories.

- Affects persons of all ages and is endemic to poor tropical nations. It can range in severity from more than light watery diarrhea to a cholera-like severe infection.
- 'Traveller's diarrhea occurs when individuals go from nonendemic to endemic.

It adheres to the intestinal mucosa primarily through fimbriae, known as colonization factor antigens, which come in various forms (CFA I, II, III, IV). ETEC generates LT, ST, or both enterotoxins (described under virulence factors).

Enterotoxins must be present in *E. coli* isolates for ETEC diarrhea to be diagnosed.

Similar to enteroinvasive *E. coli*, the 'Alkalescens-Dispar Group' (EIEC). Because they can infiltrate interstitial epithelial cells in vivo, they're dubbed enteroinvasive *E. coli*, related to shigellosis. A huge plasmid defines such capacity to infiltrate cells, and its identification may be employed as a laboratory test [8].

Enterohemorrhagic *E. coli* produces two potent toxins: verocytotoxin (VT) & Shiga-like toxin (SLT) (EHEC). These may cause diarrhea in infants and the elderly, with symptoms ranging from a bit more than light diarrhea to severe hemorrhagic colitis and hemorrhagic uremic syndrome (HUS). The main focus is endothelial cells which have a rich blood supply. This might relate to the cause of HUS, which is characterized by capillary microangiopathy, which is a prevalent kidney illness. EHEC diarrhea and its consequences are linked to *E. coli* serotype 0157: H7. 026: Hl is also included in this group [9].

The presence of VT in feces or culture isolates can diagnose VTEC diarrhea in the lab. Responsiveness can be significantly enhanced by typical and traditional or RTPCR using specific DNA probes for the VTI and VT 2 genes. On Vero or HeLa cells, the cytotoxic effects of VT may be determined. Other VTEC bacteria, unlike

most *E. coli* strains, belong to serotype 0157:H7, which cannot digest sorbitol. Consequently, testing for 0: 15 7 VTEC using the sorbitol MacConkey medium is useful [9].

Because they aggregate in a stacked brick structure on HEp-2 cells or glass, these strains are known as enteroaggregative *E.coli* (EAEC). Chronic diarrhea has been associated with them, especially in underdeveloped nations. Although most are 0-untypable, there is a handful that is H-typable [9].

Diffusely adherent *E. coli* (DAEC): These are not very well known as pathogens.

Pyogenic infections: *E. coli* mostly causes intestinal leakage-related diseases such as peritonitis and abscesses. They can even lead to pyogenic infections in the perianal region. One of the most prevalent causes of neonatal meningitis is bacteria [10].

Life-threatening infections such as "systemic inflammatory response syndrome" (SIRS) & septic shock can be caused when *E. coli* enters the circulation. Since *E. coli* usually demonstrates multiple drug resistance, antibiotic sensitivity testing of strains is critical in therapy [11].

8. PREVENTION

Despite the numerous safeguards, people can become infected by eating tainted food, particularly raw or undercooked meals. There are, however, some easy steps that may be taken to limit the chance of being unwell as a result of possibly contaminated food, animals, or another sick person. By adopting proper food handling and hand hygiene habits, consumers may frequently lower their risk of being unwell at home [12].

Personal hand hygiene is essential. Hands should be cleaned thoroughly with soap, rinsed thoroughly, and dried with a disposable kitchen towel or a textile towel (to be laundered at 60°C regularly) after managing raw vegies, roots, or meat, after contact with farm or after coming in contact with farm animals, after coming in any proximity of feces from household pets, after going to the toilet or changing nappies (diapers) or before preparing, serving or eating food [13].

Food handling

- Anyone suffering from diarrhea or vomiting should avoid handling food.
- Meat should be cooked appropriately, even minced meat.
- All fruits with skin should be peeled and cleaned thoroughly under running water.
- All veggies should be thoroughly cleaned under running water, especially those that will not be prepared before eating.
- All root veggies should be peeled and rinsed under running water.
- Cooking vegetables and meat thoroughly kill disorder-causing germs and other organisms.
- Cross-contamination, or the transmission of bacteria from raw to ready-to-eat or cooked food, may be avoided by using different cutting boards for raw and cooked meat or fresh vegetables and washing the cutting board with soap between handling raw and ready-to-eat fruits and veggies [14].

The most important step in preventing *E. coli* infection is personal hygiene and natural and surrounding hygiene. If this is taken care of, *E. coli* infections will be fewer occurrences [14].

9. TREATMENT

Currently, there are no medicines that can treat *E. coli* infection, reduce manifestations, or avoid after effects. Treatment for the vast number of people entails:

Drink plenty of water to avoid dehydration and weariness.

Avoid anti-diarrheal medications since they slow down one’s digestive system and inhibit one’s body from eliminating toxins. Antibiotics aren't generally recommended since they might increase the chances of significant problems and don't seem to neutralize the infection effectively [15].

One will be admitted to the hospital if they have a significant *E. coli* infection that has resulted in a life-threatening kind of kidney failure (hemolytic uremic syndrome). IV fluids, blood transfusions, and renal dialysis are all part of the treatment [16].

Most healthy persons may recover entirely from a STEC infection without medical treatment in approximately a week [17]. However, suppose a person has diarrhea that lasts more than three days and is accompanied by a high temperature, bloody stools, or severe vomiting that causes

dehydration. In that case, he or she should seek medical attention [18-24].

10. CONCLUSION

The study of the microbe *E. coli* has been done extensively in various ways. In studies of cytoskeleton, proliferation, and metabolic activity, it has been used as a model organism in general microbiology. It eventually became a standard method for cloning genomes from both prokaryotic and eukaryotic cells and transcription factor expression. *E. coli* is highly desirable as a regulated creature in antibiotic and decontamination effectiveness testing and a fecal infection indicator organism in edibles, water, and nature. It is an essential component of the gut microbial ecology in warm-blooded organisms and homo sapiens. It is also known that certain bacteria are antibiotic-resistant.

CONSENT AND ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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