

Pathogenesis of Escherichia coli: A clinical findings

ABSTRACT.

Introduction/Background.

Theodore Escherich, a German doctor, found *E. coli* for 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 is established by him (1894 Escherich). Until 1919 the term *Bacterium coli* was commonly used. Then after the formation of the genus *Escherichia*, Castellani and Chalmers called the type species *E. coli* (Chalmers & Castellani 1919).

Escherichia coli is the member of *Enterobacteriaceae* family and is a gram-negative facultatively anaerobic rod (with both a fermentative and respiratory metabolism) that lack oxidase production. One single rod cell of *Escherichia coli* cell is generally 1.1–1.5 μ m broad by 2–6 μ m long. They maybe motile or nonmotile, producing lateral flagella as opposed to polar flagella when motile. Many strains expand fimbriae or pili, which might be proteinaceous appendages (or structures or fibres) 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 the nature, edibles, water and intestines of many living organisms *E. coli* is a totally giant and numerous organization. Most of the *E. coli* traces are secure, some can purpose contamination. Some *E. coli* strains are chargeable for causing diarrhoea, and lots of other lines motive urinary tract infections, pneumonia, and lots of different diverse different infections and diseases.

Key words: *E.coli*, microbiology, metabolic, organism ,prokaryotic, eukaryotic, diarrhoea.

Introduction.

In the stomachs of homo sapiens and creatures with warm blood characteristics, the bacterium *Escherichia coli* (*E. coli*) is common. The broad majority of *E. coli* strains are completely 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.

Microorganism which are oxidase-negative, gram-negative, rod-shaped, 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 oxidised on triple sugar iron (TSI) or Kligler's iron agar (KIA). Although most bacteria decarboxylate lysine and utilise 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]

Pathogenic *Escherichia coli*.

E. coli strains can cause septicemia, pneumonia, meningitis, bladder and kidney infections, hemolytic-uremic syndrome (HUS), diarrhoea, and dysentery, to name a few. On the other hand, different strains with diverse combinations of 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, making them able to survive in novel surroundings and lead 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 on 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 three of the 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, which are 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 extraenteric disorders (MNEC). *E. coli* pathotypes linked in extraintestinal infections are now known as ExPEC. EPEC, EHEC, and ETEC all employ many of the same pathogens to produce sickness in animals. ^[2]

Virulence Factors.

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

Surface antigens

- **Antigen:** Endotoxic activity is caused by the somatic lipopolysaccharide O antigen . The protection of the organism against phagocytosis and bactericidal actions is mediated by complement. The envelope or K antigens in normal serum defend against phagocytosis and antibacterial agents. Antibodies to the K & O antigens stop these activities from happening . The K1 envelope antigen is carried by the *E. coli* that causes septicemia & infant meningitis , The group B antigen of meningococci is comparable with it .

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

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

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

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

- Despite the fact that 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 1 (cytotoxic necrotizing factor-1) and siderophores are important 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 , are 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) . In terms of 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 GMI ganglioside receptor present on the epithelial cells of the intestine , causing subunit A to divide into two fragments, A1 & A2 . The A1 fragment leads to activation of the adenylyl cyclase present in the enterocytes, which produces 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 up of antigenic polypeptides with a low molecular weight. STB and STA (or ST I, which is methanol soluble) are two forms of ST (or ST II, insoluble in methanol).^[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 accumulation of fluid in young piglets (age : upto 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. On plasmids, ST genes can be found with other genes such as drug resistance genes and LT genes. On the other hand, the genes STA & STB are not there on the exactly identical plasmid. ^[4]

- Verocytotoxin, commonly termed as verotoxin, which is a cytotoxic substance produced by E. coli that is affecting the Vero cells (i.e. the cell line created from kidney cells of African green monkey). Because of its physical, antigenic, and biological similarities to Shigella dysenteriae type 1 toxin, it's also recognize as Shiga-like toxin (SLT). It acts by the inhibition of the creation of proteins. VT, like Shiga toxin, causes enterotoxicity in rabbit ileal loops in addition to

producing 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 distinct VT that, unlike VT 1 and Shiga antitoxin does not neutralize it.^[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 infections of the urinary tract 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 instrumentation in hospitals.^[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 which 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]

Adhesion/Colonization.

Adhesion factors in pathogenic E. coli strains leads to the colonization of the bacteria them where it doesn't normally survive, examples the jejunum, duodenum and ileum and the urethra. The commonest morphological structures created by adhesins are fimbriae (also called pili) or

fibrillae, which may be 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 diameter of 2–4 nm. Afa adhesins, which are described as afimbrial adhesins but appear to contain a thin fibrillar part which 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 which are there on commensal *E. coli* strains can trigger signalling cascades. TLR4 binds to *E. coli* LPS and other Gram-negative bacteria's LPS, initiating a strong 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]

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 diarrhoea in babies and children, largely as a result of institutional outbreaks, but they can also cause sporadic diarrhoea 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 are neither invasive nor create enterotoxins. The plasmid-encoded protein EPEC adherence factor (EAF) has been related with 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 tropical poor nations. It can range in severity from more than light watery diarrhoea to a serious cholera-like infection.

- 'Traveller's diarrhea', which occurs when individuals go from nonendemic areas to endemic areas.

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

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

Similar to enteroinvasive E.coli, the 'Alcalescens-Dispar Group' (EIEC). Because they can infiltrate interstitial epithelial cells in vivo, they're dubbed enteroinvasive E.coli, which is related to shigellosis. Such capacity to infiltrate cells is defined by a huge plasmid, and its identification maybe employed as a laboratory test.^[8]

Enterohemorrhagic E.coli produces two strong toxins: verocytotoxin (VT) & Shiga-like toxin (SLT) (EHEC). These may cause diarrhoea in infants and the elderly, with symptoms ranging from a bit more than light diarrhoea to serious hemorrhagic colitis and hemorrhagic uremic syndrome (HUS). The main focus is endothelial cells which have rich blood supply. This might relate to the cause of HUS, which is characterised by capillary microangiopathy, which is a prevalent kidney illness. EHEC diarrhoea and its consequences are linked to E.coli serotype 0157:H7. 026:H1 is also included in this group.^[9]

The presence of VT in faeces or culture isolates can be used to diagnose VTEC diarrhoea in the lab. Responsiveness can be greatly enhanced by normal and traditional or RTPCR using specific DNA probes for the VT I 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. As a consequence, testing for 0: 15 7 VTEC using 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 diarrhoea has been associated to them, especially in underdeveloped nations. Although the most are 0-untypable, there are a handful that are H-typable.^[9]

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

Pyogenic infections: E.coli is the mostly causes intestinal leakage-related diseases such 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]

PREVENTION.

Despite the numerous safeguards in place, 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 important. 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 on a regular basis) after managing raw veggies, roots, or meat, after contact with farm or after coming in contact with farm animals, after coming in any proximity of faeces 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 diarrhoea or vomiting should avoid handling food.
- Meat should be properly cooked, even minced meat.
- All fruits with skin should be peeled and cleaned thoroughly under running water.
- All veggies, especially those that will not be prepared before eating, should be thoroughly cleaned under running water.
- All root veggies should be peeled and rinsed under running water.

- Cooking vegetables and meat thoroughly kills 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 vegies.^[14]

Most important step in prevention from E.coli infection is personal hygiene and the natural and surrounding hygiene. If this is taken care off, E.coli infections will be very less in occurrences.^[14]

TREATMENT.

There are currently 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 normally recommended since they might increase the chances of significant problems and don't seem to effectively neutralize the infection.^[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]

Without medical treatment, most healthy persons may recover completely from a STEC infection in approximately a week.^[17] However, if a person has diarrhoea that lasts more than three days and is accompanied by a high temperature, bloody stools, or severe vomiting that causes dehydration, he or she should seek medical attention.^[18-23]

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 common method for cloning genomes from both prokaryotic and eukaryotic cells, as well as transcription factor expression. *E. coli* is highly desirable as a regulate creature in antibiotic and decontamination effectiveness testing, as well as a faecal infection indicator organism in edibles, water, and the 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.

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