**Diarrhea**

Diarrhea is caused by various **viral, bacterial and parasitic** infections which are spread by ingesting contaminated food and/or water. Depending upon the adverse effects on human body, it has been categorized into distinct types: **Secretory** (poor absorption accompanied with an increase in the active secretion of anions, especially chloride ions), **Osmotic** (water is drawn into bowels due to excessive intake of sugar or salt), **Exudative** (detected by the presence of blood and pus in the stool), **Inflammatory** (associated with the loss of protein-rich fluids due to damage in the mucosal lining) and **Dysentery** (visual examination of blood in the stools).

**Causative agent**: *Escherichia coli*, Shigella, Giardia, Cryptosporidiumoocysts, Cyclospora, *Vibrio cholerae* and viruses etc.

The disease is more prevalent among children under the age of five where diarrhea is considered to be the second leading cause of infant mortality (16%) after pneumonia (17%). Reports suggest its large impact particularly in African and Asian countries as compared to the other countries. In 2011, 0.7 million deaths of children (up to the age of five) occurred due to infectious diarrhea. The scenario is more drastic in developing countries where 21% of the child mortalities occur solely due to diarrhea.

* ***E.coli***: Several strains of E. coli cause diarrhea. It has been observed that **plasmids** of these strains play a crucial role for causing the disease. The genes present in the plasmids encode for the production of **toxins** and various proteins that help the bacteria to establish itself in the host, or aid in **resistance to host** defenses. These pathogens often have **ColV** plasmid that carries genes for **two virulence determinants**. One product increases **bacterial resistance** to host defense mechanisms and the other plasmid gene synthesizes **hydroxamate** that enables E. coli to accumulate iron more efficiently from its surroundings which is essential for bacterial growth and efficient pathogenicity.

**Virulence factors**: They mainly include surface antigens and toxins (categorized into **Hemolysins and Enterotoxins**). Enterotoxins are further divided into **heat stable, heat labile and verotoxins**, which have mode of action similar to **shiga like toxins**. Further, the surface antigens include- **capsular antigen K, lipopolysaccharide antigen O and lipid A**. These factors are responsible for effective virulence of the pathogen

There are several mechanisms through which *E. coli* may cause diarrheal disease; however, **six major categories** or strains of diarrheagenic E. coli are identified that are depicted below:

**Enteropathogenic *E.coli* (EPEC):** The enteropathogenic E. coli (EPEC) strains are known to cause infantile diarrhea which is more prevalent in developing countries. The micro organisms attach to the brush border of intestinal epithelial cells where alterations in the biomolecular structure triggers a specific type of cell damage called effacing lesions. Effacing lesions or attaching-effacing (AE) lesions are represented by destruction of brush border microvilli adjacent to adhering bacteria. This cell destruction leads to water and electrolyte adsorption leading to the subsequent diarrhea .

**Enterotoxigenic *E.coli* (ETEC):** The enterotoxigenic E. coli (ETEC) strains are known to produce two types of toxins that are distinguished by their heat stability: **heat-stable enterotoxin (ST) and heat-labile enterotoxin (LT)**. These toxins bind to the proteins that are directly or indirectly associated with the intestinal epithelial cells (ST binds to a **glycoprotein receptor** and LT binds to specific **gangliosides** on the epithelial cells). ST and LT induces the production of cyclic guanosine monophosphate (**cGMP**) and cyclic adenosine monophosphate (**cAMP**) respectively which leads to the **hypersecretion of electrolytes and water** into the lumen of the small intestine, manifested as the watery diarrhea characteristic of an ETEC infection.

**Enteroinvasive *E.coli* (EIEC):** The enteroinvasive E. coli (EIEC) strains cause diarrhea by penetrating, multiplying within the colon mucosa and production of cytotoxin and an enterotoxin which leads to the excretion of mucus and blood in stool.

**Enterohemorrhagic *E.coli* (EHEC):** The enterohemorrhagic E. coli (EHEC) strains carry the genetic determinants for attaching-effacing lesions and Shiga like toxin production. It is mainly caused when under-cooked food is consumed. A major form of EHEC is the **E. coli O157:H7** that has caused many outbreaks of hemorrhagic colitis in the United States since it was first recognized in 1982.

**Enteroaggregative *E.coli* (EAEC):** The enteroaggregative E. coli (EAggEC) strains adhere to epithelial cells in localized regions, forming clumps of bacteria with a “**stacked brick**” appearance. It is responsible for both acute and chronic type where symptoms like watery diarrhea, abdominal pain, vomiting and dehydration are the most common.

**Diffusely adherent *E.coli* (DAEC):** These strains adhere diffusely over the entire surface of epithelial cells of intestine and usually cause disease in immunologically naive or malnourished children.

* **Cyclospora** is a coccidian protozoan which causes cyclosporiasis, a self-limiting diarrhea that lasts from 19 to 43 days and can be accompanied by nausea, vomiting, cramps, and fever. It occurs due to fecal contamination of imported fruits and vegetables.
* **Giardia**, a cause of human diarrhea, is one of the most common identified waterborne pathogen. In **1681, Leeuwenhoek** first observed this protozoan exhibiting trophozoite and cyst forms. The organism is known to cause “**backpacker’s diarrhea**” which spreads mainly due to unhygienic contaminated water (through untreated stream water or undependable municipal water supplies). However, various slow sand filters and slow passage of water through a bed of sand (in which a microbial layer covers the surface of each sand grain and waterborne microorganisms are removed by adhesion to the gelatinous surface microbial layer) are frequently used for the removal of **Giardiacysts** (ranging between 7 to 10 and 8 to 12 m in size).
* **Cryptosporidium** is a protozoan parasite, smaller in size than Giardia and thus it makes its removal from water even more difficult.
* ***Vibrio cholera:*** It is a waterborne pathogen which is transmitted through contaminated drinking water systems. They can be virulent because immobile hosts still shed pathogens, which frequently reach the water.

**Treatment and prevention**: Laboratory diagnosis is by isolation of the specific type of *E. coli* from feces and identification using DNA probes, the determination of virulence factors, and the polymerase chain reaction.

* Rehydration therapy by taking ORS to replace loss of electrolytes and fluids.
* Penicillin or cephalosporins, aminoglycosides, doxycycline and trimethroprim-sulfamethoxazole.
* Avoiding contaminated food and water.
* Anti-diarrheal medicine, like lomotil
* Norfloxacin, doxycycline and bactrim