8.1.6

E. Coli 0157:H7 and HUS

Watch the video *E. coli 0157:H7* Part 1 - Transmission

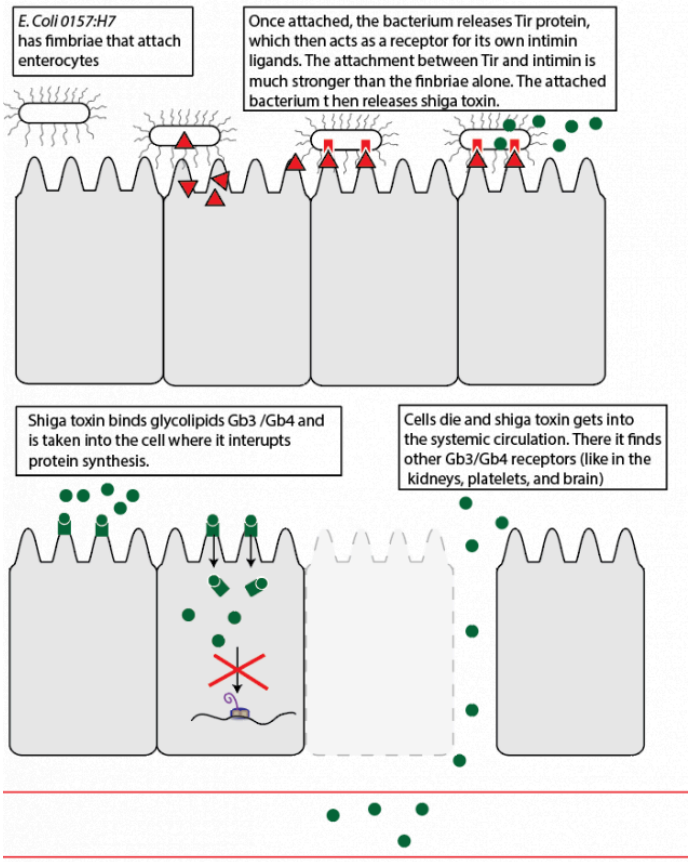
E. coli 0157:H7 is a specific strain of *E. coli* that is particularly **virulent** (which means capable of causing a disease that is severe or harmful in its effects). An infectious dose of this bacteria is only 10-100 colony forming units (cfu). This bacteria is **enterohemorrhagic**, which refers to its ability to damage the intestine and cause bloody diarrhea. It mainly affects enterocytes in the distal ileum and colon, but in severe cases it can gain access to circulation and damage other organs systems.

E. coli 0157:H7 is found in the feces of healthy livestock. It is relatively easy and possible for food to become contaminated with *E. coli 0157:H7* because these feces can be used as fertilizer for crops and cause infections in the people who eat those crops. This is part of the reason why it is important to wash the produce we eat. However, most often an infection occurs after eating meat that has been in contact with contaminated feces that contain the bacteria. It is possible that when a cow was slaughtered, there may have been feces that touched and stayed on the meat. For this reason, it is important to cook ground hamburger all the way through because the *E. coli 0157:H7* could be mixed throughout the meat. Eating rare steak is a lower risk because any *E. coli 0157:H7* would have likely only touched and stayed on the outside of the meat, which gets cooked. However, eating rare meat is not completely without risk. This is why you may see a warning on the menu at your favorite steak house that states: “WARNING: Consuming raw or undercooked meats may increase your risk of foodborne illness." *E. coli 0157:H7* can also survive in water and illness can be contracted by drinking a very small amount of contaminated water. Two locations that have increased risk for person-to-person transmission of *E.coli 0157:H7* are nursing homes and daycare centers.

Watch the video *E. coli 0157:H7* Part 2 - Pathogenesis & Complications

There are nine main steps in the pathogenesis of E. coli 0157:H7.

- Attachment of bacterial **fimbriae** to enterocyte
- Bacterial **Tir (translocated intimin receptor)** is translocated to enterocyte membrane
- Tir and the ligand **intimin** expressed on the bacteria surface bind the bacteria firmly to the enterocyte
- Release of **shiga** toxins by the bacteria
- Binding of shiga toxins to **Gb3/Gb4** receptors on enterocytes
- Shiga toxins enter enterocytes and stop protein synthesis
- Enterocyte damage and death (leads to bloody diarrhea)
- Shiga toxin gains entrance to circulation via compromised mucosa
- Damage to RBCs, platelets, kidneys, brain, and possible death can result



Process of E. coli 0157:H7 Infection *Image BYU-I JS S18*

There are many tissues in the body that express the glycolipid Gb3/Gb4. Once in systemic circulation, shiga toxin can travel to various cells in the body and attach to them via Gb3/Gb4. The attachment of shiga toxin to these glycolipids helps explain some of the well documented symptoms of **hemolytic uremic syndrome (HUS)** that can occur with an *E. coli 0157:H7* infection. For reasons not well understood, HUS is often most devastating in children as they are the population at greatest risk for developing it. HUS is defined by the simultaneous occurrence of microangiopathic hemolytic anemia, thrombocytopenia, and acute kidney injury.

- **Microangiopathic hemolytic anemia:** The kidney is at particular risk of damage by shiga toxin because of the extensive expression of Gb3/Gb4 on many cells of the kidney including glomerular endothelial cells, podocytes, mesangial cells, and tubular cells. Shiga toxin binding to these cells induces cell death in a fashion similar to what happened with the aforementioned enterocytes. The death of these kidney cells results in exposure of subendothelial elements like vWF and collagen that can activate platelets and clotting factors. Platelet plugs will form and create a meshwork of microthrombi that can damage red blood cells as they pass by, thus forming schistocytes (also called helmet cells). This increased damage to RBCs is responsible for the hemolytic anemia associated with this condition. Activation of the clotting cascade also increases risk of disseminated intravascular coagulation (DIC).
- **Thrombocytopenia:** Platelets also express Gb3/Gb4 glycolipids on their membranes. Shiga toxin adherence to platelets can trigger platelet activation and platelet plug formation. This activation and platelet plug formation causes an overall decrease in blood platelet level because they are being consumed in microthrombi formations. Thrombocytopenia results.
- **Acute kidney injury** (with uremia): Shiga toxin-induced microthrombi formations within the glomerular capillaries can occlude blood flow. Acute kidney injury can follow due to ischemic damage and decreased glomerular filtration. This condition can be observed by the accumulation of urea in the blood (uremia) because this waste product cannot be eliminated by healthy kidney filtering processes.

It is sometimes possible to see neurological manifestations of systemic shiga toxins that include stroke, seizures, coma, and hemiparesis. This is because Gb3/Gb4 is also expressed in brain tissue, so shiga toxin can bind and cause organ damage in a similar manner to what happens in the kidney. Moreover, microthrombi that form in other parts of the infected body may travel to the brain and become lodged in the microcirculation, causing ischemia.

Treatment of an *E. coli 0157:H7* infection mainly consists of supportive care with a focus on rehydration. The use of antibiotics and antidiarrheal agents during the early stages of diarrhea from an *E. coli 0157:H7* infection are not recommended because they increase the risk of HUS. Antibiotics increase the risk because they cause the gut to be exposed to a greater amount of toxins as the bacteria are killed. Antidiarrheal agents increase the risk because they inhibit the body's efforts to flush out the bacteria.