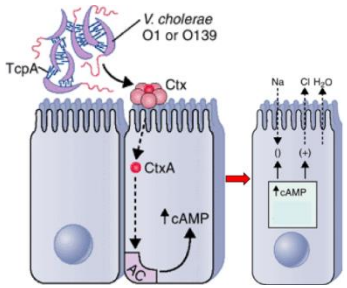
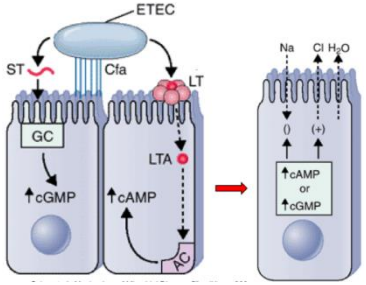
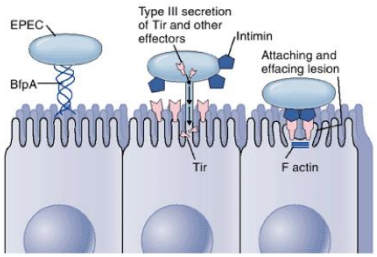
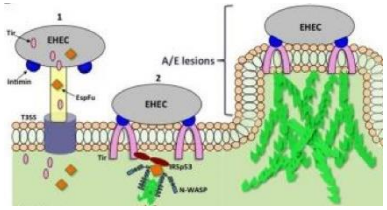
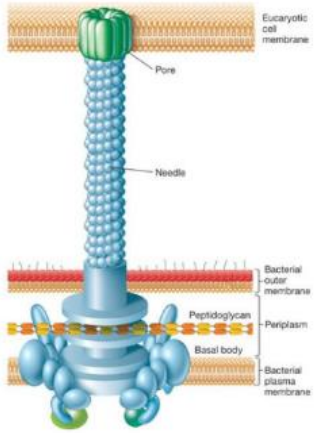
Non-invasive (extracellular) gastro enteritic bacteria

	Vibrio cholerae	Enterotoxigenic *E. coli* (ETEC)
Distribution	Global distribution, mostly developing countries, lives water and humans.	Infants and travellers in developing countries. Outbreaks from contaminated food in developed countries.
Information	-Serotype O1 (LPS Ag) subdivided into 2 biotypes – classical and El Tor. -Serotype O139 (non-O1 serotype).	
IP, ID	**IP:** 4 – 24 hours.	**IP:** 14 – 30 hours. **ID:** High (10^8 cells).
Transmission	Contaminated food and water.	Contaminated food and water.
Effects	-Profuse watery diarrhoea and dehydration. -Death if not treated.	-Mild, watery diarrhoea and abdominal cramping. -Occasionally fever and vomiting.
Adhesion mechanism	**Toxin coregulated pili (TCP):** Fimbrial adhesin mediates attachment. These pili allow intestinal colonisation and allow binding and forming of micro-colonies.	**Colonisation factor antigen (CFA):** Fimbrial adhesin for colonisation of gut epithelium.
Damage mechanism	**Cholera toxin (AB_5):** -The cytotonic toxin binds to GM1 gangliosides (surface receptors on intestinal cells). -A cleaves into A1 and A2 subunits, A1 internalised via endocytosis. -A1 subunit increase cAMP levels and adenylate cyclase activity. -Increase in NaCl in lumen causes osmotic secretion of water. 	**Heat liable toxin (LT):** Identical to the cholera toxin. **Heat stable toxin (ST):** Different structure, but similar function to the cholera toxin. 
Diagnosis	**Culture:** Thiosulfate Citrate Bile salts Sucrose agar (TCBS). -37˚C, 24-48 hours. -Forms yellow colonies (others form green colonies). -Biochemical and serological identification used to fully characterise.	**Culture:** MAC, DCA. -37˚C, 24 hours. **PCR:** Identify LT and ST producing genes.
	Vibrio parahaemolyticus -Natural inhabitant of marine waters – contaminated and undercooked shellfish. -IP of 12-24 hours. -Produces watery diarrhoea, nausea, vomiting and abdominal cramps. -Invasive pathogen. -Grows on TCBS (green colonies).	

	Enteropathogenic *E. coli* (EPEC)	Enterohaemorrhagic *E. coli* (EHEC)
Distribution	Most cases occur in children and neonates in developing countries.	Developed countries, cattle reservoir (zoonosis).
Information		Major serotype O157:H7.
IP, ID	**IP:** 6-48 hours. **ID:** High (>10^6 cells).	**IP:** 1-8 days.
Transmission	Contaminated food and water.	Contaminated, undercooked meat.
Effects	Acute, profuse, protracted watery diarrhoea.	Dysentery (bloody diarrhoea).
Adhesion mechanism	**Bundle forming pili (Bfp):** Fimbrial adhesin encoded of EAF plasmid, mediates loose attachment to enterocytes. **T3SS**: Inserts Tir receptors to allows binding of Intimin for intimate attachment to the enterocytes (afimbrial). 	**Adhesins:** Unknown. **T3SS:** Tir and other effector proteins injected, Intimin then mediates intimate attachment (afimbrial). **Pedestal formation:** Caused by actin rearrangement in host cell cytoplasm. 
Damage mechanism	T3SS causes destruction villi (through A/E lesions), increasing intestinal permeability leading to diarrhoea.	**Shiga toxins Stx1 & Stx2 (AB_5):** Binds to Gb3 receptors and causes damage to vasculature of intestine.
Diagnosis	**Culture:** MAC, DCA**.** -37˚C, 24 hours. **PCR:** For *bfpA* and *eae* (intimin). **Immunofluorescent microscopy:** Actin staining test.	**Culture:** MAC, Sorbitol MAC, special chromogenic agars. **Serological tests:** EIA for Shiga toxins. **PCR**: For *eae* (intimin) and Shiga toxins.
		EAggEC: Causes watery, persistent diarrhoea in infants less than 6 months old.

Type III Secretion System (T3SS): Needle and syringe mechanism for translocating virulence proteins from microbe to host cell cytoplasm (widespread amongst GN animal and plant pathogens).

- **EPEC:** Delivers Tir, which binds Intimin outer membrane protein.
- **Shigella:** Delivers effector protein Ipa to induce uptake by epithelial cells.
- **Salmonella:** Encodes 2 T3SS for invasion and intracellular survival.
- **Yersinia:** Delivers proteins for distribution of the innate immune system.



Invasive GE bacteria

	Shigella spp.	*Salmonella spp.*
Distribution	-Developing countries – *S. dysenteriae.* -Young adult males – *S. flexneri.* -Industrial countries – *S. sonnei.* -Other – *S. boydii.*	Worldwide due to normal flora of many animals.
Information	-Lactose non-fermenting, non-motile. -Human-only.	-Lactose non-fermenting. -Can cross species.
IP, ID	**IP:** 8-72 hours. **ID:** Low (10^2, acid stable).	**IP:** 8-72 hours. **ID:** High (acid labile).
Transmission	Direct person to person.	Contaminated food and water.
Invasion mechanism	-Uptake into M cells in not well known, but does required Ipa **T3SS:** Delivers Ipa (Invasion Plasmid Antigens) to induce membrane ruffling for uptake into basal surface of enterocytes. **IcsA (Intracellular Spread):** Recruits host cell actin which facilitates cell to cell spread.	**T3SS (1):** Delivers Sips (Salmonella invasion proteins from SPI-1) to induce membrane ruffling and uptake into M cells and enterocytes.
Infection cycle	-Shigella approaches Microfold cells. -Invades M-cells following Ipa injection or passes through junctions between enterocytes. -Bacteria is released into the lamina propria and engulfed by macrophages (inflammation is triggered, neutrophils migrate to area). -Neutrophils migrating through the mucosal tissues cause separation of the cell junctions, which causes more invasion of bacteria. -Some bacteria escape macrophages and invade adjacent cells through phagolysosome uptake. -Bacteria lyse phagolysosome, allows replication in the cytoplasm. -ICSA protein induces actin polymerisation to allows invasion of neighbouring cells without moving extracellularly, host cell dies.	-Target Microfold cells. -SIPs induce cellular mediators and mobilise intracellular calcium which induces membrane ruffling and bacteria uptake by cellular mediators. -Cellular mediators also cause an electrolyte accumulation in lumen and inflammation leading to diarrhoea. -Bacteria escape at basal surface, causing no harm. -Can be engulfed by macrophages (and also dendritic cells). -**T3SS (2):** Delivers SSAs (Salmonella survival antigens from SPI-2) for survival inside vacuole of macrophage. -Transported to lymph nodes, some may escape into blood stream.
Damage mechanism	**Focal ulcer:** Invaded cells die. **Shiga toxins Stx (AB_5):** Cytotoxic toxin binds Gb3 receptors on underlying blood vessels, inhibiting protein synthesis and eventually cell death.	-No damage caused due to bacteria escaping through basal surface. -Electrolyte accumulation in lumen and inflammation cause diarrhoea.
Diagnosis	**Culture:** MAC, DCA. -Detect LNF (distinguish from regular *E. coli*), no H_2S production. **Biochemical tests:** Aids identification -Serotyping of cell wall (O) antigens. -No flagella (H) antigens.	**Culture:** MAC, DCA. -Detect LNF, yellow colonies (black due to H_2S production). **Biochemical test, slide agglutinations:** Confirm identity **Phage typing, gel electrophoresis, genome sequencing:** Allows for strain comparison

	Yersinia enterocolitica	*Campylobacter*
Distribution	Worldwide.	Worldwide, animal reservoir.
Information		-Microaerophilic. -Curved, GN rods.
IP, ID		**IP:** 2-4 days. **ID:** High (acid labile).
Transmission	Spread via unpasteurised milk and undercooked meat.	Contaminated water (and milk) and food.
Invasion mechanism	**OMP:** Invasin protein (afimbrial) contains motif which help bacterium bind to host cell surface β_1 integrins.	
Infection cycle	-Bacteria invades M cells. -Engulfed by macrophage. -Apoptosis of macrophage releases bacteria, to further invade. -Can cause local and systemic dissemination.	Not well understood.
Damage mechanism	**T3SS:** Delivers Yop (Yersinia outer proteins) proteins which causes cytotoxicity, induce apoptosis and also inhibits many innate immune responses.	-Can produce bloody diarrhoea. **Guillain Barre syndrome:** Immune-mediated polyneuropathy.
Diagnosis	**Culture:** MAC, CIN. -LNF (MAC). -Bulls eye (CIN). **Urease:** Positive. **Oxidase:** Negative.	**Culture:** CAMP. -42˚C, 48 hours, microaerophilic. **Gram stain, microscopy:** Gram negative curved rods.

AB_5 toxin comparison

Shiga toxin (EHEC and Shigella dysenteriae 1): Acts on endothelial cells to inhibit protein synthesis – cytotoxic.

Cholera toxin and LT toxin of ETEC: Act in intestine to increase cAMP – secretory diarrhoea, cytotonic.