

enterobacteriaceae

intro.

- 1) >50 genera + 100s of species + sub.
- 2) ubiquitous (soil, water, vegetable + intestinal flora of humans + animal)
- 3) non-spore forming
- 4) gram -ve rod
- 5) facultative anaerobes
- 6) moderate sized
- 7) species + sub. share common AG enterobacterial common AG
- 8) it can be:
 - A) Normal intestinal flora
 - B) always associated with disease
 - C) opportunistic infections
 - D) normally commensal that become pathogenic when they acquire virulence genes.

virulence factor

- 1) endotoxin → lipid A of LPS, released at cell lysis
- 2) capsule → hydrophilic AG → repel phagocytic cells but Anticapsular Antibiotics diminish the capsule role
- 3) Antigenic phase variation (alternately expressed or not):
 - A) somatic O Antigen
 - B) capsular K antigen
 - C) flagella H antigen
- 4) Type 3 secretion system
- 5) counteract iron sequestration by producing their own siderophores or iron chelating compound (enterobactin, aerobactin) or from iron released from lysed cells
- 6) resistance to serum killing + antimicrobial resistance

Antibiotic resistance

- 1) resist Antibiotic esp β -lactam type
- 2) increasingly dominated by the mobilization of continuously expressed single genes that encode efficient drug modifying enzymes
- 3) there's shift of the natural resistance membrane impermeability, drug efflux to modern paradigm of mobile gene pools that transmit resistance between bacteria
- 4) Carbapenem resistant enterobacteriae (CRE):
produce carbapenemase → disable the drug
→ resistant to carbapenemase (moderate-severe)
- 5) CRE can kill 1/2 of patient who get bloodstream
- 6) main risk factor for CRE acquisition in USA including exposure to healthcare + to Antibiotics

classification

depend on 3

- 1) biochemical properties
- 2) AG structure
- 3) molecular analysis of genome
- 4) protein composition by mass spectrometry

enterobacteriaceae

E. coli

intro.

- 1) most extensively studied type
- 2) most common + imp. member of the genus *Escherichia*
- 3) can be both:
 - A) commensal inhabitant of GIT
 - B) one of most imp. pathogens

E. coli strains

- 1) Commensal strains innocuously colonize the colon of healthy host. cause extraintestinal disease only in the presence of a large inoculum ex: with penetrating abdominal trauma or/4 significant host compromise
- 2) Diarrhoeagenic strains → diarrhoea syndrome syndrome that vary in clinical presentation + pathogenesis according to the strain's distinctive virulence traits
- 3) Extraintestinal pathogenic E. coli (ExPEC) often innocuously colonize the human gut. but they have a unique ability to enter + survive within normally sterile e. intestinal body site → cause disease there.

Enterotoxigenic E. coli (ETEC)

disease

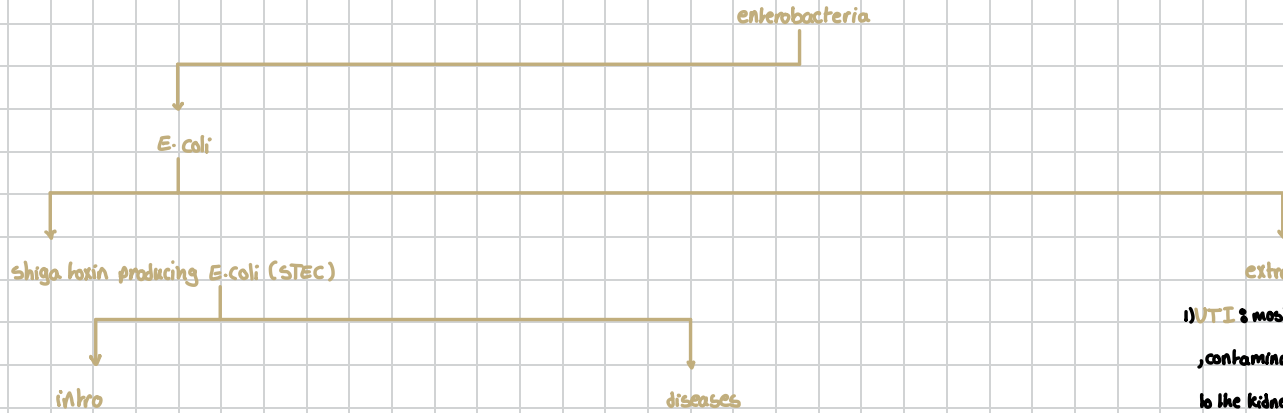
- 1) one of most common cause of bacterial diarrheal disease
- 2) 30% of traveler's diarrhea
- 3) acquired through fecally contaminated water or food
- 4) person to person → X
- 5) 1-2 days (incubation period) + persists for 3-5 days
- 6) symptoms:
 - A) secretory diarrhea (water, non-bloody)
 - B) abdominal cramps
 - C) Nausea + vomiting (less common)

toxin

- 1) Heat stable:
 - ↑ cGMP + subsequent hypersecretion of fluid + inhibition of fluid absorption
- 2) Heat labile:
 - ↑ cAMP → enhanced secretion of chloride + ↓ absorption of sodium + chloride

Note:

it can be fatal in undernourished patient



- 1) most infection → consumption of undercooked meat products + water + unpasteurized milk or fruit juices + uncooked vegetable + fruits
- 2) ingestion of <<100 bacteria → disease
- 3) person to person → occurs
- 4) 3-4 days of incubation within 2 days of onset
- 4) disease in 30-65% of patient progresses into with bloody diarrhea with severe abdominal pain
- 5) complete resolution of symptoms typically occurs after 4-10 days in most untreated patient

- A) mild uncomplicated diarrhea to hemorrhagic colitis with severe abdominal pain + bloody diarrhea
- B) severe → associated with STEC O157:H7
- C) HUS → acute renal failure, thrombocytopenia + Microangiopathic hemolytic anemia, is complication in 5% to 10% of infected children younger than 10y



extraintestinal infections

- 1) UTI & most -ve rod that produce UTI originate in the colon, contaminate the urethra, ascend into the bladder + may migrate to the kidney or prostate
- 2) women more affected UTI (*E. coli* → 80% of cases)
- 3) men are affected by cystitis, less frequently
- 4) neonatal meningitis & *E. coli* + group B streptococci cause the majority of CNS infections in infant <= one month
- 5) septicemia & typically caused by gram -ve rods (*E. coli*) most commonly originate from infection in urinary + GI + high mortality rate in immunocompromised patient



disease:

- * S. Typhi → febrile illness called typhoid fever
mild form → paratyphoid fever by S. paratyphi
- * enteric fever:
Back → pass through the cells + engulfed by macrophage + replicate before reaching liver, spleen + bone marrow
10-14D after ingestion → ↑ fever, malaise, myalgias + anorexia + nonspecific complaints of headache
- * treated with fluoroquinolones

enterobacteriae

Shigella

intro.

- 1) dysenteriae, flexneri, boydii, sonnei (Sh.)
after DNA analysis → 4 species are actually biogroup within species of E. coli.
- 2) cause disease by invading + replicating in cells lining colon.
- 3) structural gene protein mediate the adherence of the organisms to the cells + their invasion, intracellular replication + cell to cell spread
- 4) Humans are the only reservoir

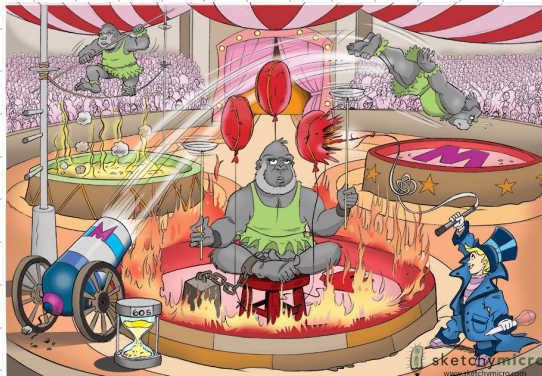
toxins

- 1) shiga toxin → dysenteriae (exotoxin)
- 2) A sub of shiga → cleaves 28s rRNA in the 60s ribosomal → prevent binding of aminoacyl-tRNA + disrupting protein synthesis
- 3) primary manifestation of toxin activity → damage to the intestinal epithelium. However, in small subset of patients → damage to the glomerular endothelial cells → renal failure (HUS)

diseases

shigellosis

- * pri. pediatric disease, 60% of patients are children < 10y
- * transmitted person to person
- fecal-oral route
- * abdominal cramps, diarrhea
- fever + bloody stool
- * signs disappear 1-3 D after bacteria is ingested
- * self-limited, Antibiotic is recommended → ↓ risk of sec. spread to family members



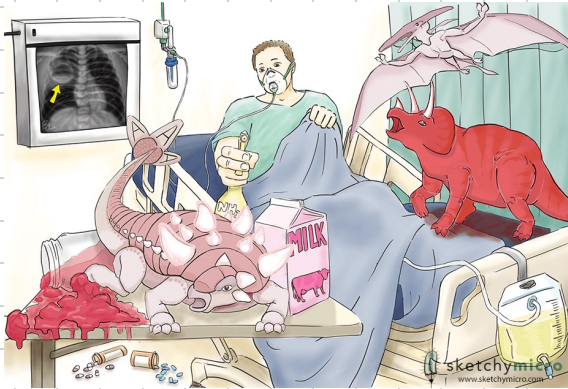
Shigella passes the epithelial cell (EC) barrier by **transcytosis** through M cells and encounters resident macrophages. The bacteria **evade degradation in macrophages by inducing an apoptosis-like cell death**, which is accompanied by proinflammatory signaling. Free bacteria **invade the EC** from the basolateral side, **move into the cytoplasm by actin polymerization**, and spread to adjacent cells. Proinflammatory signaling by macrophages and EC further activates the innate immune response and attracts PMN. The influx of PMN **disintegrates the EC lining**, which initially exacerbates the infection and tissue destruction by facilitating the invasion of more bacteria. Ultimately, PMN phagocytose and kill Shigella, thus contributing to the resolution of the infection.

enterobacteriae

klebsiella

intro.

- 1) routinely found in the human nose, mouth, GI as normal flora
- 2) most common member is *K. pneumoniae* which cause community or hospital acquired **pri. lobar pneumonia**.
- 3) also cause **wound + soft-tissue infections + UTIs**
- 4) *K. pneumoniae* → coloize the hospital environment + carpeting + sinks + flowers + surface



proteus

intro.

- 1) *P. mirabilis* → most common mem.
+ produce infection of **urinary tract**
- 2) *P. mirabilis* produce ↑ [urease]
→ ↑ PH of urine → precipitating
 Mg^{2+} , Ca^{2+} in the form of struvite
, apatite crystals respectively
→ formation of **kidney stone**
- 3) ↑ alkalinity of urine is also
toxic to uroepithelium



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Yersinia

intro

- 1) best-known human pathogen is *Y. pestis*
- 2) all infections are zoonotic with human
- the accidental host infections
- 1) urban plague & rats are reservoirs
- 2) sylvatic plague & in squirrels, rabbits, field rats + domestic cats
- * The patients are highly infectious & person to person spread occurs by aerosols in case of pneumonic plague

3 major pandemic

- 1) Justinian plague & affected much of mediterranean basin - virtually all of the known world at that time.
- 2) Great plague (sec pandemic) black death
- 3) modern plague (3rd pandemic) spread by rats on steamship

disease

- Bubonic plague &
 - * caused by *Y. pestis*
 - * incubation < 7D after a person has been bitten by an infected flea
 - * high fever, painful bubo (inflam. swelling of lymph nodes) in the groin or axilla
 - * Bacteremia → untreated, 75% die

