









TEAM443
MICROBIOLOGY

Normal flora and introduction to infectious diarrhea

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Objectives

-  Recall the common microbiota of the GIT
-  Understand the role of the microbiota of the GIT in diseases.
-  Describe the epidemiology, risk factors & host defenses in preventing GI infections.
-  Describe various types of acute diarrheal illnesses, the pathogens that cause them, their clinical presentation, pathogenic mechanism and prevention.
-  Explain the pathogenesis of E.coli, Campylobacter, Yersinea & Clostridium difficile and their management.
-  Discuss microbiological methods used for the diagnosis of common bacterial agents causing diarrheal infection.

Any future corrections will be in the editing file, so please check it frequently

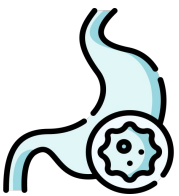
Color Index:
Main text
Important
Doctor Notes
Males slide
Females slide
Extra



Microbiota of the GI

Introduction {1}

- Microbiota are microorganisms that are frequently found in various body sites in normal healthy individuals. (basically they are normal flora)
- Constituents and number vary according to the age and physiologic status.
- Able to colonize & multiply under the existing condition of different body sites
- Inhibit competing intruders.
- Have symbiotic relationship that benefit the host.
- Can cause disease in immunocompromised patients.



Normal flora of GIT



Colon of adults

10^{10} org/g stool, >90% are **Bacteroides (anaerobic)**, 10% other bacteria. (most common place)



Saliva

contain mixed microbiota:
 10^8 /ml



Small intestine

very scanty (poor) except near colon



Oral cavity

contains high number of microbiota which vary from site to site of the mouth.

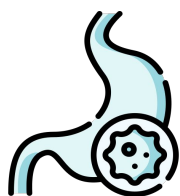


Stomach

has **limited microbiota** due to HCL and peptic enzymes

Other

Direct effect of diet composition.



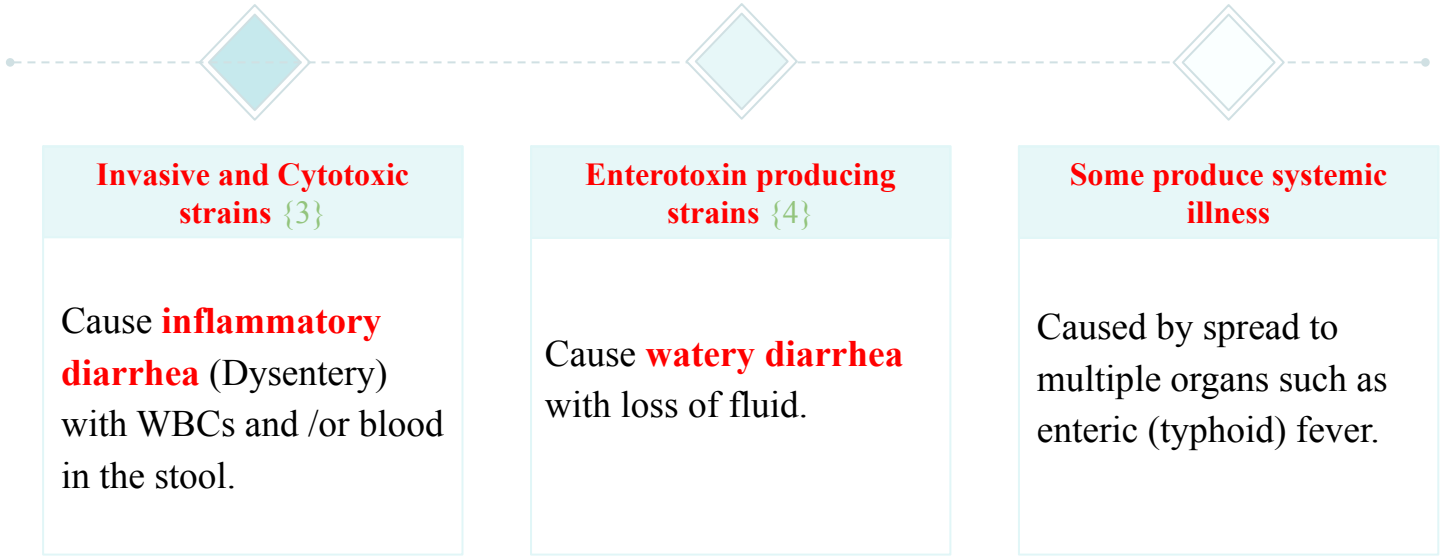
Microbiota of the GI

| | Microbiota (low virulence) | Potential pathogen (carrier) |
|------------------------|--|--|
| Mouth | <ol style="list-style-type: none"> 1. Viridans streptococci 2. Neisseria spp 3. Moraxella 4. Peptostreptococcus. | 1-Candida albicans |
| Nasopharynx | <ol style="list-style-type: none"> 1. Neisseria spp 2. Viridans sterpt 3. Moraxella 4. Peptostreptococcus. | <ol style="list-style-type: none"> 1. S.pneumoniae 2. N.meningitidis 3. H.influenzae 4. S.pyogenes, S.aureus (In nose) |
| Stomach | <ol style="list-style-type: none"> 1. Streptococci 2. Peptostreptococcus 3. others from mouth. | none |
| Small intestine | scanty, variable | none |
| Colon | <ol style="list-style-type: none"> 1. Bacteroides 2. Fusobacterium, Eubacterium 3. Lactobacillus 4. Enterobacteriaceae 5. Clostridium, Enterococcus | <ol style="list-style-type: none"> 1. B.fragilis, E.coli 2. Pseudomonas, Candida, 3. Clostridium (C. perfringens, C.difficile) |

| Role of microbiota in disease | Role of microbiota in diarrheal disease {2} |
|---|---|
| Many are opportunistic pathogens , eg. perforation of the colon from ruptured diverticulum (distribution of the normal anatomy), feces enter into peritoneal cavity and cause peritonitis | E.coli : the most common Enterobacterales; a facultative flora of colon followed by Klebsiella, Proteus and Enterobacter. |
| <ul style="list-style-type: none"> - Viridans streptococci of oral cavity enters the blood and infects damaged heart valves. - Mouth microbiota play a role in dental caries. | Salmonella, Shigella and Yersinia are NOT microbiota of the intestinal tract. |
| <ul style="list-style-type: none"> - Compromised defense systems increase the opportunity for invasion. - Death after lethal dose of radiation due to massive invasion of microbiota. | Some strains of E.coli ,Salmonella ,Shigella and Yersinia enterocolitica are able to cause diseases in the intestinal tract.(they always cause a disease) |



Intestinal Pathogens



Acute Diarrheal Illnesses & Food Poisoning

| | | |
|--------------------------------------|---|---|
| <p>Introduction {5}</p> | <ul style="list-style-type: none"> ◦ Acute diarrheal illness is one of the most common problems evaluated by clinicians ◦ A major cause of morbidity and mortality worldwide. (especially in children) ◦ Most of healthy people have mild illness but other might develop serious sequelae so it is important to identify those individuals who require early treatment. | |
| <p>Definition of diarrhea</p> | <ul style="list-style-type: none"> ◦ Stool weight in excess of 200 gm/day, or three or more loose or watery stools/day ◦ Alteration in normal bowel movement ◦ characterized by decreased consistency and increased frequency ◦ Less than 14 days in duration. | |
| <p>Etiology {6}</p> | <p>Viral</p> | <p>70-80% of infectious diarrhea in developed countries (mostly self limiting and inflammatory diarrhea)</p> |
| | <p>Bacterial</p> | <p>10-20% of infectious diarrhea but responsible for most cases of severe diarrhea (might require a treatment)</p> |
| | <p>Protozoan</p> | <p>less than 10%.</p> |
| <p>Epidemiology</p> | <ul style="list-style-type: none"> ◦ 1.2 - 1.9 episodes per person annually in the general population ◦ 2.4 episodes per child <3 years old annually ◦ 5 episodes per year for children <3 years old and in daycare ◦ Seasonal peak in the winter. | |



Diarrhea

Classification ★

| Method of causing infection | Infectious Diarrhea {7} | Intoxication {8} | Traveler Diarrhea | Antibiotic Associated Diarrhea |
|-----------------------------|---|--|---|--------------------------------|
| Caused by | Viral or Bacterial infections (eg. <i>Campylobacter</i> , <i>Shigella</i> , <i>Salmonella</i> , <i>Yersinia</i> , <i>Vibrio cholerae</i> & <i>E.coli</i>). -the organism itself gets ingested- | <i>Staphylococcus aureus</i> , <i>Bacillus spp.</i> (The toxin itself is already present in food and it gets ingested) | mainly caused by Enterotoxigenic E.coli. | <i>Clostridium difficile</i> |

Clinical Presentation & Pathogenic Mechanisms:

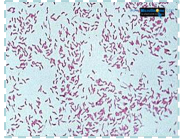
| | <u>Enterotoxin mediated</u> Entero=in the GI {11} | Invasive and/or cytotoxin production |
|-----------------|---|---|
| Stool | Lack of pus in the stool (no gut invasion) (almost always watery) | Pus and blood in the stool (not always bloody sometime cause watery diarrhea) |
| Symptoms | No fever, Vomiting, non-bloody diarrhea, abdominal cramps. | Fever due to inflammation |
| Etiology | <i>Vibrio cholerae</i> , <i>Staphylococcus aureus</i> , <i>Bacillus cereus</i> (organisms in red are the most common and most rapid), <i>Clostridium perfringens</i> and Some viral and parasitic infections. | <i>Shigella</i> , <i>Salmonella spp.</i> , <i>Campylobacter</i> , some <i>E.coli</i> and <i>Entamoeba histolytica</i> |
| Location | Affect the small intestine . | Affect colonic mucosa |
| Characteristics | Some have rapid onset (<12 hour if due to preformed toxin ingestion) (So intoxication diarrhea is the most rapid form of diarrhea) | -Extension to lymph nodes -Incubation period 1-3 days -Dysentery syndrome -gross blood and mucus -EHEC bloody diarrhea - <i>Entamoeba histolytica</i> 1-3 wk |

Risk factors

- 1 Food from restaurant
- 2 Being in contact with a Family member with gastrointestinal symptoms
- 3 Recent travel to developing countries
- 4 Patient underlying illness and medication, low stomach acidity, cyst, spores (immunocompromised or any issues on GIT)
- 5 Abnormal peristalsis
- 6 Median infective dose (ID50) {9}
- 7 Low Immunoglobulin A (IgA),
- 8 Antibiotics decrease the normal flora to less than 10^{12} {10}



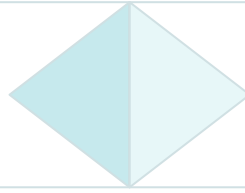
Campylobacter

| Campylobacter | |
|------------------------------|--|
| Aspect | Information |
| Morphology {12} | <ul style="list-style-type: none"> ○ Gram negative curved (spiral or S-shape) bacilli  |
| Common species | <ul style="list-style-type: none"> ○ C.jejuni, C. coli, C fetus. |
| Source {13} | <ul style="list-style-type: none"> ○ dog , cat, birds, poultry(Chicken products),water, milk, meat, person to person transmission can occur. |
| Clinical Presentation | <ul style="list-style-type: none"> ○ worldwide infection ,more common among children ○ Incubation period: 2-6 days ○ Lower abdominal pain , watery or dysenteric diarrhea with pus and blood. ○ fever in some patients ○ Nausea and vomiting are rare ○ Self limiting after 2-6 days. ○ Chronic carrier & outbreaks uncommon. |
| Complications | <ul style="list-style-type: none"> ○ May lead to autoimmune disease like Guillain-Barrie' syndrome and extra-intestinal infections eg. reactive arthritis ,bacteremia ,lung infection and others frequently preceded by C.jejuni infection. |
| Lab Diagnosis | <ul style="list-style-type: none"> ○ Culture on special media ○ Use transport media ○ Culture on CAMPY BAP media containing antibiotics. ○ Incubate in microaerophilic atmosphere (5%O2 , 10%CO2 , 85%N) at 42°C except C.fetus 37°C ○ Identification :Gram stain, culture ,biochemical & Serology. |
| Treatment | <ul style="list-style-type: none"> ○ Recommended only for severe cases ○ Erythromycin or Ciprofloxacin . |
| Pathogenic mechanism | <ul style="list-style-type: none"> ○ Mainly by invasion |



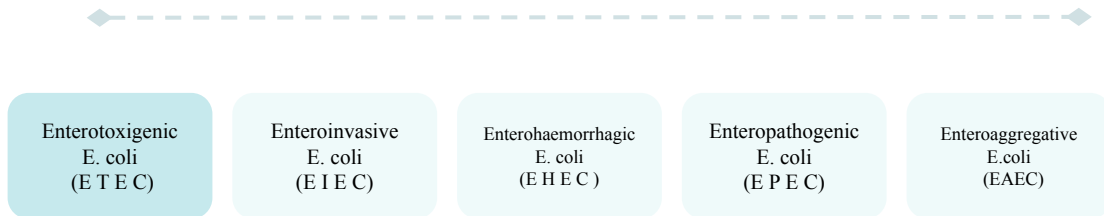
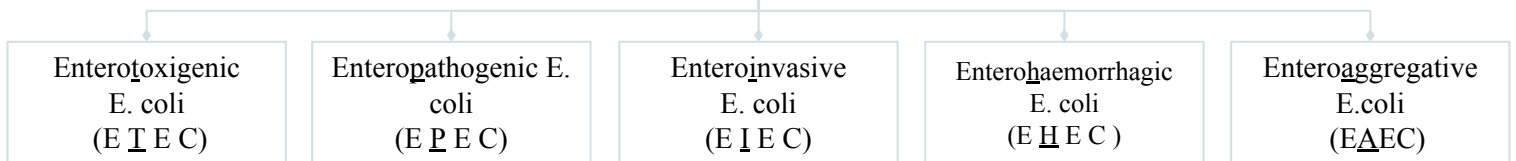
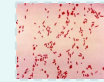
E.Coli

About 10 -15% of strains of E. coli associated with diarrhea. Other strains associated with extra-intestinal diseases (septicemia, meningitis & **UTI**).



Based on **virulence factors**, clinical manifestation, epidemiology and **different O and H serotype**. {14}

Types of Diarrheagenic E. coli

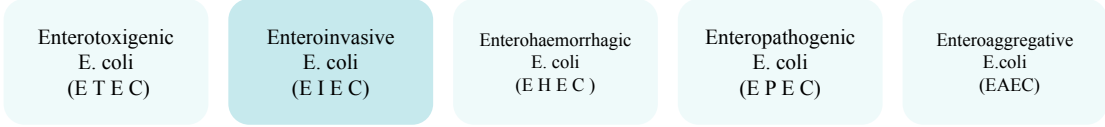


| Aspect | Information |
|----------------|--|
| Disease | Major cause of Traveler's diarrhea in infant and adult in developing countries due to consumption of contaminated food and water . {15} |
| Infective Dose | It has high infective dose $10^6 - 10^{10}$ |
| Toxin | <ul style="list-style-type: none"> It produces two types of toxins, the toxin will affect the absorption and lead to watery diarrhea Produce heat-labile toxin (LT) and heat-stable toxin (ST), each has two fragment (A and B). No invasion or inflammation. LT leads to accumulation of cyclic CAMP, which leads to hyper-secretion of fluid with no cellular injury |
| Symptoms | <ul style="list-style-type: none"> watery diarrhea abdominal cramps and some time vomiting . |
| Treatment {16} | <ul style="list-style-type: none"> Usually Self limiting . Person with traveler diarrhea can be treated to reduce symptoms |
| Diagnosis | No routine diagnostic method required. |

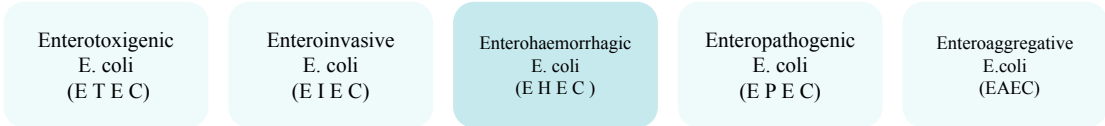
(The **t** in **toxigenic** link it with the **t** in **TRAVEL**)



E.Coli



| Aspect | Information |
|----------------|---|
| Disease | <ul style="list-style-type: none"> ◦ Produce dysentery (Penetration, invasion and destruction). Mainly seen in children. ◦ Similar to Shigella Spp. (non motile, NLF) How similar? |
| Infective Dose | High Infective dose 10^6 |
| Transmission | Fecal oral route . |
| Symptoms | Fever, severe abdominal cramp, malaise and watery diarrhea |



| Aspect | Information {17} ★ |
|---------------|--|
| Disease | <ul style="list-style-type: none"> ◦ 0157:H7 {19} Hemorrhagic diarrhea, colitis and hemolytic uremic syndrome (HUS) manifested with low Platelet count, hemolytic anemia and kidney failure |
| Prevalence | Fatal disease in young and elderly persons in nursing homes (Because of HUS not because of the diarrhea) |
| Etiology {18} | <p>Undercooked hamburgers, unpasteurized dairy products, Apple cider, cookie dough</p> |
| Toxin | <ul style="list-style-type: none"> ◦ Cytotoxin: Shiga-toxin I & II (verotoxin I and verotoxin II) (Similar to toxin produced by <i>Shigella dysenteriae</i>) ◦ E.coli other than 0157:H7 can cause HUS. |
| Symptoms | <ul style="list-style-type: none"> ◦ Bloody diarrhea ◦ low grade fever and stool with no leukocytes |
| Management | Management of HUS required. Antimicrobial therapy not recommended . Because it increase the risk of bacteria producing the toxine |
| Diagnosis | Diagnosis by culture on " special media" SMAC(sorbitol MacConkey agar), Vertoxin detection by immunological test or nucleic acid testing (NAT). |



E.Coli

Enterotoxigenic
E. coli
(E T E C)

Enteroinvasive
E. coli
(E I E C)

Enterohaemorrhagic
E. coli
(E H E C)

Enteropathogenic
E. coli
(E P E C)

Enteraggregative
E.coli
(EAEC)

| Aspect | Information {20} |
|------------|--|
| Disease | <ul style="list-style-type: none"> ◦ Cause infantile diarrhea (bottle fed infants) ◦ Disrupt microvilli and intestinal absorptive function. |
| Prevalence | Outbreak in hospital nurseries and day care centers |
| Symptoms | <ul style="list-style-type: none"> ◦ watery diarrhea ◦ Low grade fever, malaise, vomiting ◦ mucous in stool but no blood. |

Enterotoxigenic
E. coli
(E T E C)

Enteroinvasive
E. coli
(E I E C)

Enterohaemorrhagic
E. coli
(E H E C)

Enteropathogenic
E. coli
(E P E C)

Enteraggregative
E.coli
(EAEC)

| Aspect | Information |
|--------------|--|
| Disease | Pediatric diarrheal disease |
| Pathogenesis | Adhering to the surface of the intestinal mucosa. Produce aggregative stacked brick . |
| Symptoms | <ul style="list-style-type: none"> ◦ Produce mucoid, watery diarrhea ◦ vomiting, dehydration and abdominal pain |
| Prognosis | May resolve after two weeks or more . |

The Alien from the Pathology took a trip to Microbiology just to ask you this :

What is the mechanism of action of LT enterotoxin?

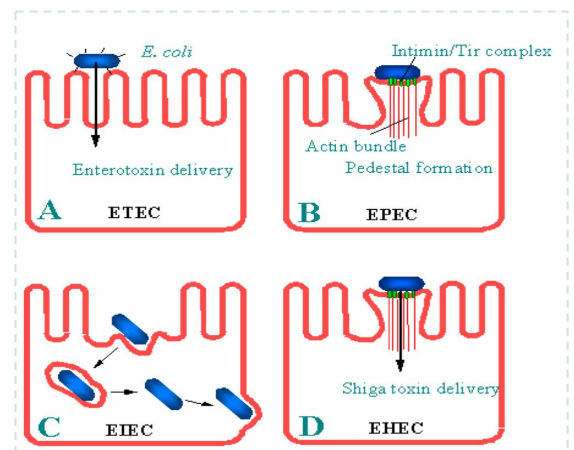
- Decreases secretion of fluids and electrolytes, leading to cell lysis
- Activates adenylate cyclase to increase cAMP concentrations
- Decreases Cl absorption, increases Na secretion
- Inhibits the 60s subunit of ribosomes
- Increases levels of cGMP in the intestine

Answer: B

Which of the following is NOT a common cause of E. coli infection?

- Contaminated irrigation of fruits and vegetables
- Manure contamination of food
- Improper food preparation/handling
- Contaminated respiratory droplets
- Contaminated drinking water

Answer: D





Clostridium difficile

| Aspect | Information |
|------------------------------|---|
| Morphology | <ul style="list-style-type: none"> ◦ Gram-positive Bacilli ◦ Anaerobic spore forming (live on surfaces/important in hospitals) |
| Disease | <p>Antibiotic associated diarrhea (ampicillin, cephalosporins clindamycin) (broad spectrum that doesn't cover c.difficile) Antibiotic used during the last 8 weeks (community acquired) or hospital stay for at least 3 days (hospital acquired) produce spores to pt must be isolated.</p> |
| Pathogenesis | <ul style="list-style-type: none"> ◦ the risk factor of clostridium difficile is exposed to chemotherapy and antibiotic, that lead to decrease normal Flora present in small intestines → give the bacteria chance to grow and replicate and release toxin. ◦ the clostridium difficile is both cytotoxin and enterotoxin can cause either watery or bloody diarrhea. |
| Transmission | from person to person via fecal-oral route |
| Prevalence | Cultured from inanimate hospital surfaces. |
| Toxin | <ul style="list-style-type: none"> ◦ Disruption of the endogenous bacterial flora of the colon ◦ Produce toxin A (enterotoxic & cytotoxic effects) and B (cytotoxic) is the main toxin which binds to surface epithelial cell receptors leading to inflammation ,mucosal injury and diarrhea. (usually watery but potentially can be bloody) |
| Symptoms | Patient presents with fever, leukocytosis , abdominal pain and diarrhea |
| Treatment | <ul style="list-style-type: none"> ◦ oral (Better than IV)Vancomycin or fidaxomicin and supportive treatment ◦ Notify infection control |
| Diagnosis {21} | direct toxin detection from stool by enzyme immunoassay (EIA), or toxin gene detection by NAT. |
| Histological findings | <p>Pseudomembrane can result (neutrophils, fibrin, and cellular debris in the colonic mucosa) and toxic megacolon</p> <p>A colon section from died pt.Notice the inflammation, pus formation and haemorrhage.</p> |

C.difficile & pseudomembranous colitis





Yersinia Enterocolitica

| Aspect | Information {22} |
|------------------------|--|
| Morphology | <ul style="list-style-type: none"> ○ Gram negative bacilli ○ Non lactose fermenter ○ Oxidase negative |
| Disease | Causes mesenteric lymphadenitis in children and septicemia in immunocompromised hosts |
| Epidemiology | Rare in ksa. Common in Europe, USA, Canada .Cat, dog, swine (chitterlings) Chitterlings are a prepared food usually made from small intestine of a pig |
| Symptoms | Presented with enteritis, arthritis and erythema nodosum Erythema nodosum is a type of skin inflammation that is located in a part of the fatty layer of skin |
| Characteristics | <ul style="list-style-type: none"> ○ Survive cold temperatures and associated with transfusion of packed red blood cells. ○ Generalized infection in adult and children 1-5 year, usually mild but in old children and adult mimic appendicitis |
| Diagnosis | Growth at 25°-30°C, media: Cefsulodin-Irgasan- Novobiocin (CIN media) |



Lab Diagnosis

Lab Diagnosis of Diarrheal Diseases caused by bacteria :

| | |
|-----------------------|--|
| Stool specimen | <p>Culture:</p> <ul style="list-style-type: none"> ○ on selective media for Salmonella, Shigella & Campylobacter. Culture for Vibrio Cholerae, EHEC or Yersinia If suspected. |
| | <p>Toxin assay:</p> <ul style="list-style-type: none"> ○ if C.difficile toxins is suspected. |
| | <p>Nucleic acid amplification testing</p> <ul style="list-style-type: none"> ○ NAATs detect genetic material (nucleic acids) |



Which of the following symptoms is NOT seen with hemolytic uremic syndrome?

- Kidney failure
- Lysis of red blood cells
- Thrombocytopenia
- Damage to small blood vessels
- Bloody sputum

Answer: E



Summary From the Slides

Selected Clinical and Epidemiologic Characteristics of Typical Illness Caused By Common Foodborne Pathogens*

| Pathogen | Typical Incubation period | Duration | Typical Clinical Presentation | Assorted Food |
|-------------------------|---------------------------|-------------|---|---|
| Salmonella species | 1-3 Days | 4-7 Days | Gastroenteritis | Undercooked eggs or poultry, produce |
| Campylobacter jejuni | 2-5 Days | 2-10 Days | Gastroenteritis | Undercooked poultry, unpasteurized dairy products |
| E.Coli Enterotoxigenic | 1-3 Days | 3-7 Days | Gastroenteritis | Many foods |
| Shigella species | 1-2 Days | 4-7 Days | Gastroenteritis | Produce, egg salad |
| Listeria monocytogenes | 2-6 weeks | Variable | Gastroenteritis, meningitis abortion | Deli meat, hotdogs, unpasteurized dairy products |
| Bacillus cereus | 1-6 hour | <24 hour | Vomiting, Gastroenteritis | Fried rice, meats |
| Clostridium botulinum | 12-72 hour | Days-months | Blurred vision, paralysis | Home-canned foods, fermented fish |
| Staphylococcus aureus | 1-6 hour | 1-2 Days, | Gastroenteritis, particularly nausea | Meats, potato & pork, unpasteurized dairy products. |
| Yersinia enterocolitica | 1-2 Days | 1-3 weeks | Gastroenteritis, appendicitis-like syndrome | Undercooked pork, unpasteurized dairy products. |



1. normal flora have symbiotic relationship that benefit the host as present of normal flora make difficult to other organism to cause infection, but the problem it can cause infection in immunocompromised patient
2. Salmonella, Shigella and Yersinia are NOT normal flora of the intestinal tract. They are potentially pathogenic, while bacteria E.coli are considered microbiota and there is a lot different type of it some causes UTD and other cause gastroenteritis depending on virulence factor they have
3. there are two types of disease pathogenesis in gastrointestinal tract pathogens especially bacteria:
 1. invasive and 2. cytotoxic production, they causes bloody diarrhea because they cause inflammation and invasive lead to potentials blood “not always have blood”

➤ **Another explanation from group B:**

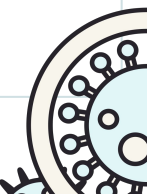
1. Invasive Toxins:

- Definition: Invasive toxins are substances produced by pathogens that aid in their ability to invade and spread within host tissues.
- Mechanism: These toxins often facilitate the penetration of the pathogen into host cells or tissues by disrupting cellular barriers or immune responses.
- Examples: Invasive toxins can include enzymes that break down host cell membranes or factors that interfere with the host's immune system to promote the pathogen's survival & spread.

2. Cytotoxins:

- Definition: Cytotoxins are toxins that specifically target and damage cells, leading to cell death (cytotoxicity).
- Mechanism: Cytotoxins may disrupt cellular structures, interfere with cellular functions, or induce programmed cell death (apoptosis). Their primary effect is on the host cells rather than facilitating invasion.

4. and also we have enterotoxin producing strain pathogenesis this produce toxin that lead to release more fluid in stool → watery diarrhea
5. the diarrhea in general it common and usually is mild self limiting, but it have probably to be severe in areas with low resources, old people, also in children because they don't have oral hydrate solution and usually it difficult to keep them hydrated
6. infection diarrhea mainly cause by viruses and most of them are self limiting, and if cause by bacteria the are also self limiting but some of them require treatment in case caused severe manifestations or in immunodeficiency patients
7. infection diarrhea mean ingested pathogen contaminated with water or food and then start to cause infection according to pathogenic mechanism of pathogen itself either bacteria or viruses.
8. intoxication process mean eating the toxin it self, in other words the toxins itself is already present in the food and it gets ingested, so because of that they have incubation period faster than infection diarrhea
9. Median infective dose (ID50) is a measure used to represent the amount of a pathogen required to infect 50% of the subjects, Some organisms causes symptoms with lower number of organisms (low ID50) and vice versa. On other words infective dose is to describe the number of organisms are required to cause diseases, Some of organism can cause symptoms with low estimated number of organisms while other need high number to produce symptoms, in our block we have only three bacteria have low infectious dose salmonella typhoid type and shigella, enterohemorrhagic E Coli.
10. Antibiotics decrease the normal flora so that will leave a space for infectious organisms





11. in Enterotoxin mediated bacteria the Patient either
 - A. ingests the toxin itself so the incubation period and symptoms comes very quick. For example, present food contamination with staph. Aureus (while preparation with inwash hand/or keep the food exposed in room temperature/ eat from open buffet meals) → heat stable toxin is released → patient eats it → diarrhea & severe vomiting 1 hr later and ,so staph. Aureus it is common in food poisoning and causes severe acute diarrhea.

Note The toxin was produce by S.aureus is heat stable toxin so when you keep the food exposed and then heating,the toxine are still present and not effect even the bacteria dey
 - B. or ingest the organism that will then multiply and release toxins within the body so the incubation period and symptoms become longer . For example you ingest Vibrio cholerae & clostridium perfringens From see food which probably contaminated, then it will replicate and release toxin (So the ingested pathogen itself Will start the pathogenic process)
12. campylobacter microbiology it has same character of helicobacter, but the presentation & diagnosis are different, both of them are -Ve bacilli & microaerophilic & oxidase positive.
13. mainly the most common cause of campylobacter from poultry or ingested item related to poultry or use contaminated knife to cut the chicken or salt.
14. as we mentioned before the epidemiology and clinical manifestation of E.coli strains changes depending on O(somatic polysaccharide) and H (flagellar) antigens,and E.coli is considered the most common cause of UTI
15. Enterotoxigenic E.coli are the Major cause of Traveler's diarrhea in infant and adult in developing countries,it is normally present with water but in this country are present in higher amount because of that it lead to cause diarrhea , that why in traveling to some country are not recommended to drink or wash vegetables in tap water rather than use bottled water.
 - in enterotoxigenic E.coli why do you that the residents of the country do not get diarrhea? because the residents of the country have acquired immunity, and the person who goes there also has immunity, but it is temporary, so it is possible that if he goes there a second time, he will get diarrhea.
16. usually enterotoxigenic E.coli are self limiting but there are some recommend treatment to decrease duration of symptoms
17.
 - Enterohemorrhagic E.coli is the most important of E.Coli cause diarrhea due it lead to severe manifestation out GIT
 - Enterohemorrhagic E.coli is the only one can come from human due it have low infection dose
18. Enterohemorrhagic E.coli, used to be called Hamburger disease due it commonly caused by Undercooked hamburgers (ground beef) but it can be also from unpasteurized dairy products, Apple cider or cookies
 - Why only hamburgers? Why not steak? Because steak is not minced مفروم (only the outer surface is exposed to the bacteria and it will be exposed to heat). However, in the case of hamburger, beef will be minced and also contaminate the inner portion of the meat (it needs to be cooked very well & reach a certain temperature)
19. O157 somatic antigen :H7 (flagella) is the most common serotype of EHEC
 - used to be called Hamburger disease however it's caused by any burger not only ham
20. enteropathogenic E.coli it can cause disease by produce lesions called attaching and effacing lesion on small intestine → affected the absorptive function →watery diarrhea
21. diagnosis done by direct toxin detection from stool by enzyme immunoassay (EIA), or toxin gene detection by Nucleic acid implication, can we do culture? yes we can do culture ○ specially but mainly aren't use do it expensive and take time
22.
 - yersinia enterocolitica aren't common in our country because the main source are swine
 - and it cultured on specific media with low temperature



Summary

Intestinal Pathogens

Invasive and Cytotoxic strains

Cause **inflammatory diarrhea** (Dysentery)

Enterotoxin producing strains

Cause **watery diarrhea** with loss of fluid.

Some produce systemic illness

Caused by spread to multiple organs such as typhoid fever.

Note :Salmonella, Shigella and Yersinia are NOT microbiota of the intestinal tract.

Diarrhea

Acute Diarrheal Illnesses & Food Poisoning

| | | |
|-------------------------------|---|---|
| Introduction | <ul style="list-style-type: none"> Acute diarrheal illness is one of the most common problems evaluated by clinicians A major cause of morbidity and mortality worldwide.(especially in children) | |
| Definition of diarrhea | <ul style="list-style-type: none"> Stool weight in excess of 200 gm/day, or three or more loose or watery stools/day Alteration in normal bowel movement | |
| Etiology | Viral | in developed countries (mostly self limiting and inflammatic diarrhea) |
| | Bacterial | responsible for most cases of severe diarrhea (might require a treatment) |
| Classification | Infectious Diarrhea | Viral or Bacterial infections (eg. Campylobacter , Shigella, Salmonella , Yersinia, Vibrio cholerae & E.coli). -the organism itself gets ingested- |
| | Intoxication | Staphylococcus aureus, Bacillus spp. (The toxin itself is already present in food and it gets ingested) |
| | Traveler Diarrhea | mainly caused by Enterotoxigenic E.coli . |
| | Antibiotic Associated Diarrhea | Clostridium difficile |
| Risk Factors | 1.Food from restaurant 2.Being in contact with a Family member with gastrointestinal symptoms 3. Recent travel to developing countries 4. Median infective dose (ID50), 5. Antibiotics decrease the normal flora | |

Clinical Presentation & Pathogenic Mechanisms:

| | Enterotoxin mediated Entero=in the GI | Invasive and/or cytotoxin production |
|------------------------|---|--|
| Stool | Lack of pus in the stool (no gut invasion) (almost always watery) | Pus and blood in the stool (not always bloody sometime cause watery diarrhea) |
| Symptoms | No fever,, non-bloody diarrhea, | - |
| Etiology | Vibrio cholerae, Staphylococcus aureus, Bacillus cereus | Shigella, Salmonella spp., Campylobacter, some E.coli and Entamoeba histolytica |
| Characteristics | Some have rapid onset (<12 hour if due to preformed toxin ingestion) So intoxication diarrhea is the most rapid form of diarrhea | - |



Summary

Extra

Pathogens

E. coli (Based on virulence factors, clinical manifestation, epidemiology and different O and H serotype)

| | Disease | Etiology | Toxin | Symptoms | Treatment | Diagnosis |
|------------------------------|--|---|--|---------------------------------|-------------------------|---|
| Enterohaemorrhagic E. coli ★ | 0157:H7, colitis and hemolytic uremic syndrome (HUS) manifested with low Platelet count, hemolytic anemia and kidney failure | Undercooked hamburgers, unpasteurized dairy products, Apple cider | Cytotoxin: Shiga-toxin I & II (verotoxin I and verotoxin II) | Bloody diarrhea | Management of HUS | culture on special media, Verotoxin detection by immunological test or nucleic acid testing |
| Enterotoxigenic E. coli | Traveler's diarrhea in developing countries due to consumption of contaminated food and water. | - | Produce heat-labile toxin (LT) and heat-stable toxin (ST) | watery diarrhea | Usually Self limiting . | - |
| Enteroinvasive E. coli | <ul style="list-style-type: none"> Produce dysentery (invasion). Similar to Shigella Spp. (non motile, NLF) How similar? | - | - | - | - | - |
| Enteropathogenic E. coli | Cause infantile diarrhea | - | - | watery diarrhea | - | - |
| Enteraggregative E.coli | Pediatric diarrheal disease | - | - | Produce mucoid, watery diarrhea | - | - |

Other

| | Transmission | Toxin | Disease | Symptoms | Treatment | Characteristics |
|---|---|---|---|---|--------------------------------|--|
| Campylobacter (C.jejuni, C. coli) Curved bacilli | dog, cat, birds, poultry (chicken products) | - | May lead to Guillain-Barrie' syndrome, reactive arthritis, bacteremia | Lower abdominal pain, watery or dysenteric diarrhea with pus and blood. | only for severe cases | - |
| Clostridium difficile ★ | from person to person via fecal-oral route | Produce toxin A (enterotoxic & cytotoxic effects) and B (cytotoxic) | Antibiotic associated diarrhea, hospital acquired | fever, leukocytosis and diarrhea | oral Vancomycin or fidaxomicin | -Pseudomembrane can result and toxic megacolon -diagnosis by direct toxin detection from stool by enzyme immunoassay (EIA), or toxin gene detection by NAT. |
| Yersinia Enterocolitica | - | - | mesenteric lymphadenitis | Presented with enteritis, arthritis & erythema nodosum | - | mimic appendicitis |



MCQs

| | | | |
|--|-----------------------------|-----------------------|----------------------------|
| 1- what is the causative organism of traveller's diarrhea ? | | | |
| A- EHEC | B- EPEC | C- EIEC | D- ETEC |
| 2- which of the following diseases will be complicated into Guillain-Barre syndrome ? | | | |
| A- Rhinitis | B- pseudomembranous colitis | C- Campylobacteriosis | D- Cholera gravis |
| 3- which of the following of GIT is mostly colonized by normal flora? | | | |
| A- Colon | B- stomach | C- small intestine | D- oral cavity |
| 4- which of the following organisms cause food poisoning ? | | | |
| A- Streptococcus pneumonia | B- EHEC | C- Vibrio cholera | D-staphylococcus aureus |
| 5- which of the following species can cause antibiotic associated diarrhea? | | | |
| A- Enteroaggregative E.coli | B- Clostridium difficile | C- staph aureus | D- Yersinia enterocolitica |
| 6- Enteroaggregative E.coli can cause watery diarrhea with mucus secretion by which of the following mechanisms ? | | | |
| A- distribution of endogenous bacterial flora of colon | B- stacked bricked villi | C- villi disruption | D- Cytotoxic mediated |

8-9
8-5
4-7
A-3
C-2
D-1



SAQ

Case 1

A 30 years old visited an outpatient clinic with diarrhea for 2 days after eating chicken barbecue. The culture showed gram-negative curved bacilli.

Q1: mention the causative organisms?
Campylobacter

Q2: mention other causative organism?
Salmonella

Q3: How is the campylobacter causes disease?
mainly through invasive

Case 2

60-years old seen in emergency with bloody diarrhea and start to have high creatinine, anemia thrombocytopenia.

Q1: what caused these symptoms for the patient?
Enterohemorrhagic E.coli

Q2: what is the effected gene?o157:H7

Q3: mention an associated syndrome that comes with the disease?
Haemolytic uremic syndrome

Q4:what is the most likely source?
Undercooked ground beef or contaminated dairy products

Q5: What is the appropriate treatment ?
Supportive care

Q6: what is pathogenic mechanisms ?
Production Shiga-toxin I & II

Case 3

A five people gone to buffet meet, 2 hours later four of them started to have severe vomiting, abdominal cramps and mild diarrhea.

Q1: what is the form of the infection ?
pathogenesis through enterotoxin and we called this process (toxification)

Q2: what is the causative organism ?
Staphylococcus aureus
- another causes organism is bacillus and it associated with rice, however the S. aureus is usually most common

Case 4

7 years old came to the emergency with pneumonia admitted ceftriaxone and erythromycin. One week later started to have watery diarrhea and high blood cell count and fever.

Q1:what is the most likely causative organism?
Clostridium difficile

Q2: what is the pathogenic mechanism?
Antibiotic use & disruption of normal flora → exposure to clostridium → colonization → multiplication→ toxin B production (causes cell destruction/perforation/dilation) → diarrhea (watery/bloody).

Q3:what is the diagnostic method?
detection of toxins by EIA and toxin gene by molecular test



TEAM 443
MICROBIOLOGY

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