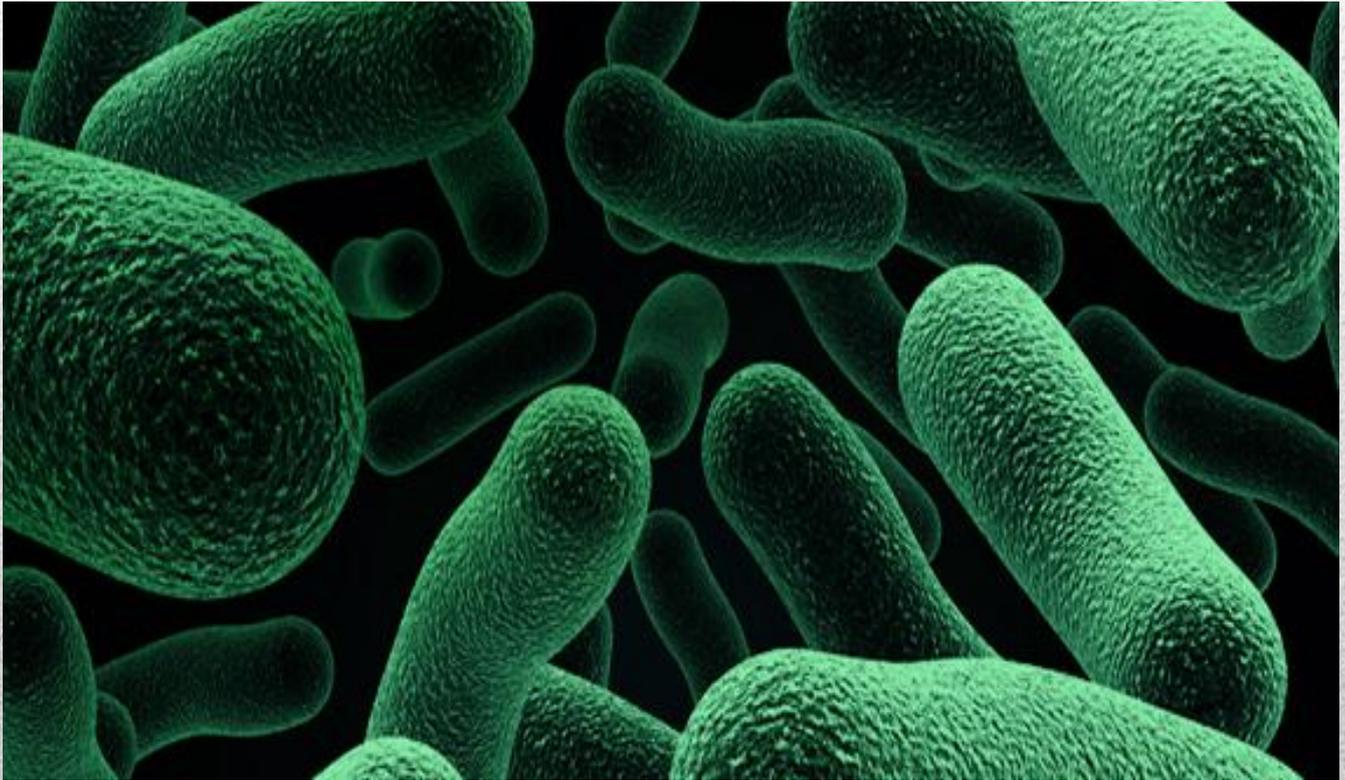




## Lecture 2

# Normal Flora & introduction of Infectious Diarrhea



*Microbiology team 430*

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## Normal Flora

- **Def:** Normal flora is microorganisms that are frequently found in various body sites in normal, healthy individuals.
- Colon containing the largest number of normal flora (about  $10^{10}$  org/gm), while the stomach contains the minimal number because of the presence of HCL (so pt on anti acidic drugs is more susceptible to get infection).
- NF could enter the blood (due to dental procedures) causing damage to the heart valve (endocarditis).
- It also could go to peritoneum (due to surgery or rupture of the bowl) causing peritonitis.

### Definition of Diarrhea:

- Alteration in normal bowel movement with **decreased consistency** and **increased frequency**.
- Three times a day in less than 14 days.
- It is self limiting but sometimes it requires an early treatment.

## Intestinal Pathogens

- **Invasive and cytotoxic strains** → causing **inflammation** which result in = [ **Dysentery** ] " WBCs, blood, mucous and pus are found in stool"
- **Enterotoxin** Strains = **watery diarrhea** and loss of fluids.

**Enterotoxin:** causes alteration in electrolytes, resulting in  $\uparrow$  of cl in the intestinal lumen followed by  $\uparrow$  in  $H_2O$  causing watery diarrhea.

### ❖ Etiology:

- Viral:** very **serious in children** less than 3 years old. (**most common**)
- Bacterial:** responsible for most cases of severe diarrhea, very common in adults.
- Protozoan:** less than 10%.

### ❖ Classification:

- **Infectious diarrhea:** Viral (e.g. **Rota virus – most common**), Bacterial (e.g. **Campylobacter, Shigella, Salmonella, Yersinia, Vibrio cholerae, E.coli**)
- **Food poisoning:** **Staphylococcus aureus, Clostridium perfringes, Bacillus spp.**
- **Traveler diarrhea:** **Enterotoxogenic E.coli.**
- **Antibiotic associated diarrhea:** **Clostridium difficile.**

### ❖ Risk Factors

- Family member with gastrointestinal symptoms.
- Food from restaurant.
- Recent travel to developing countries.
- **Low stomach acidity or antacids drugs.**
- Abnormal peristalsis.
- Low Immunoglobulin IGA.
- **Antibiotics** = decrease the normal flora.

## Clinical Presentation and Pathogenic

### ❖ Mechanism I:

- **Enterotoxin mediated** (watery diarrhea):
- **Clinical presentation:**
  - No pus in the stool (because of no invasion).
  - Lack of fever.
  - Vomiting non-bloody diarrhea, abdominal cramp.
  - **Rapid onset, Incubation period (IP) is 6 – 18 Hrs (short).**
- **Affects: Small intestine.**
- **Pathogens: Vibrio cholerae, Staphylococcus aureus, Clostridium perfringens and Bacillus cereus.**

- Toxins produced by organism are resistance to heat.

### ❖ Mechanism II :

- **Invasive** (dysentery):
- **Clinical presentation:**
  - Pus and blood in the stool.
  - Fever due to inflammation.
  - Extension of lymph nodes.
  - **Dysentery syndrome- gross blood and mucous**
  - **Incubation period 1-3 days (long)**
- **Affect: colonic mucosal surface of the bowel (large colon).**
- **Pathogens:**
  - **Shigella, Salmonella spp., Campylobacter**, some E.coli and Entameba histolytica
  - Entameoba histolytica 1-3 wk
  - **EHEC bloody diarrhea (EHEC: Enter Hemorrhagic E-Coli)**

## Campylobacter

- **Family: Campylobacteraceae.**
- **Genus: Archobacter.**
- **Description: Spiral Gram negative bacilli [Rods].**
- **Common species: C. jejuni, C. coli, C fetus.**
- **Source: dog, cat, birds, poultry [like chicken] →water, milk, meat, person to person can occur.**

### ❖ Clinically:

- **IP 2-6 days. (Or 1-3 days – because it is an invasive organism).**
- **Very common and mild.**
- **Presentation: Abdominal cramp, bloody diarrhea, nausea and vomiting are rare.**
- **Self limiting.**
- **Guillain-Barre syndrome [GB ] is the most common complication**

### ❖ **Laboratory diagnosis:**

- Transport media Cary Blair.
- CAMPYBAP media contain antibiotics.
- It needs Oxygen to grow → because of that, it's incubated in a media containing 5% O<sub>2</sub> 10% CO<sub>2</sub> 85% N at 42°C media except C.fetus 37°C. (called microaerophilic).
- **Gram stain** /Serology (for Identification)

CAMPYBAP: simply it is a blood agar containing antibiotics

### ❖ **Treatment:**

- **Erythromycin** [Macrolides].

## ***E.coli***

- There are five major categories of diarrheagenic E.coli:

<b>Pathogen</b>	<b>Infection</b>
- <b>Enterotoxigenic E. coli (ETEC).</b>	Traveler's diarrhea
- <b>Enteropathogenic E. coli (EPEC).</b>	Infantile diarrhea
- <b>Enteroinvasive E. coli (EIEC).</b>	Dysentery (blood & mucus)
- <b>Enterohaemorrhagic E. coli (EHEC).</b>	Bloody diarrhea (very severe)
- <b>Enteroadherent E. coli (EAEC).</b>	Pediatric diarrheal disease (same as EPEC)

All diarrhea caused by E.coli are **self limiting** (no treatment).

### ❖ **Enterotoxigenic E.coli :**

- Major cause of **traveler's diarrhea** in infant and adult in developing countries from contaminated food and water.
- It has high infective dose 10<sup>6</sup>-10<sup>10</sup>
- Produces **two types of toxins: heat labile toxin (LT) and heat stable toxin (ST)** both are A&B type.
- **Symptoms: watery diarrhea**, abdominal cramps and some time vomiting.
- **Diagnosis:** No routine diagnostic method.

A&B type: means that the toxin has two parts: A part → which is an infectious part & B part → which is a carrier

### ❖ **Enteroinvasive E.coli:**

- Produce **dysentery** (Penetration, invasion and distraction)
- Infective dose 10<sup>6</sup>
- It produces **Shigella-like toxin**.
- Fecal oral route
- **Symptoms:** Fever, severe abdominal cramp, malaise and watery diarrhea
- **Diagnosis:** Sereny test and DNA probes.

### ❖ **Enteropathogenic E.coli:**

- **Infantile diarrhea [ Infants ]**
- Outbreak in **hospital nurseries** and day- care centers.
- Low grade fever, malaise, vomiting and diarrhea
- **Mucous in stool but no blood.**

### ❖ *Enterohemorrhagic E. coli:*

- Serotype: 0157:H7 → Hemorrhagic diarrhea, colitis and hemolytic uremic syndrome, hemolytic anemia and kidney failure.
- **Symptoms:** Bloody diarrhea, low grade fever and stool have no leucocytes.
- **Source:** Undercooked hamburgers, unpasteurized dairy products, apple cider, cookie dough → This bacteria lives in cows' intestine
- **Diagnosis:** by culture, MUG test, immunological test or PCR
- Produces two types of Cytotoxin = Verotoxin I and Verotoxin II similar to (shiga-toxin I & II)
- Fatal disease in young and elderly persons in nursing homes.
- *Very dangerous in children because its presentation is mild then it progress to bloody diarrhea.*

### ❖ *Enteroadherent E. coli:*

- Pediatric diarrheal Disease.
- Adhering to the surface of the intestinal mucosa and can cause UTI.
- Watery diarrhea, vomiting, dehydration and abdominal pain for 2 or more weeks

## *Yersinia enterocolitica*

- Mesenteric lymphadenitis in children and septicemia in immunocompromised hosts.
- Chitterlings [intestine of pigs] are the most common site.
- It's rare in the middle-east but very common in North America.
- Survive cold temperatures and associated with transfusion of packed red blood cells.
- Presented with enteritis, arthritis and erythema nodosum.
- Generalize infection in adult and children 1-5 yrs, usually mild but in old children adult mimic appendicitis.

## *Clostridium difficile*

- Antibiotic associated diarrhea.
- Transmit from person to person via fecal-oral route.
- Have been cultured from inanimate hospital surfaces.
- Disruption of the indigenous bacterial flora of the colon.
- Produces A&B type of toxin.
- **Clinical Presentation:** fever, leukocytosis, abdominal pain and diarrhea.
- Pseudomembrane can result (neutrophils, fibrin, and cellular debris in the colonic mucosa) and toxic megacolon.
- **Diagnosis:** toxin detection by enzyme immunoassay (EIA).
- Treatment Metronidazole ± Vancomycin and supportive treatment.

## *Summary:*

- Diarrhea is defined as Alteration in normal bowel movement characterized by decreased consistency and increased frequency.

- There are two types of strains that cause diarrhea:
  1. **Invasive strains = dysentery** (due to **inflammation**) contains **WBCs (pus), blood and mucous.**
  2. **Enterotoxin Strains = watery diarrhea and loss of fluids.**
- **Causes of infectious diarrhea are:** Viral (**most common especially rota**), bacterial [**Campylobacter, Yersinia, Vibrio cholerae, E.coli**] or protozoal infections.
  - Bacteria that cause Food poisoning are: ***Clostridium perfringens, S. Aureus and Bacillus cereus.***
- **Antibiotic associated diarrhea** is caused by **Clostridium difficile**
- The most important risk factors of acute diarrhea are: **low stomach acidity, Antibiotics and decreased food and personal hygiene.**
- **Enterotoxin mediated** mechanism is **very rapid; IP is 6 – 18 Hrs** and takes place in the **small intestine** and causes **watery diarrhea.**
- **Invasive** mechanism is **slower; IP is 1 – 3 days**, takes place in the **colon** and causes **Dysentery.**
- **Campylobacter:**
  - **Spiral Gram –ve bacilli.**
  - Most common species is **C.jejuni.**
  - Most common source is **Poultry [Chicken].**
  - **Self-limiting, microaerophilic [requiring oxygen for growth but at lower concentration than is present in the atmosphere]**
  - Complication: **Guillain-Barré syndrome.**
  - Diagnosis: **Gram stain.**
  - Treatment: **Erythromycin “ Macrolides”**

○ **E.coli:**

<b>Pathogen</b>	<b>Infection</b>
- <b><u>Enterotoxigenic E. coli</u> (ETEC).</b>	<b>Traveler's diarrhea</b>
- <b><u>Enteropathogenic E. coli</u> (EPEC).</b>	<b>Infantile diarrhea</b>
- <b><u>Enteroinvasive E. coli</u> (EIEC).</b>	<b>Dysentery (blood &amp; mucus)</b>
- <b><u>Enterohaemorrhagic E. coli</u> (EHEC).</b>	<b>Bloody diarrhea (very severe)</b>
- <b><u>Enteroadherent E. coli</u> (EAEC).</b>	<b>Pediatric diarrheal disease (same as EPEC)</b>

- Serotype 0157:H7 of EHEC will cause **hemorrhagic diarrhea, colitis, hemolytic uremic syndrome (HUS), hemolytic anemia and kidney failure**
- EHEC Produces **verotoxin 1 & 2**, which is similar to ( **shiga toxin 1&2**)
- ETEC produces **heat labile toxin (LT) and heat stable toxin (ST).**
- **Yersinia enterocolitica:** most commonly found in **Chitterlings [intestine of pigs]**, causes:
  - **Mesenteric lymphadenitis.**
- **Clostridium difficile:** It causes **Antibiotic associated diarrhea, Pseudomembranous colitis** and treated by **Metronidazole.**
- **Listeria monocytogenes** has the **longest IP (2-6 weeks)** and found in **cheese (dairy products)** and it causes **Gastroenteritis and meningitis.**
  - **Clostridium botulinum** causes **paralysis and blurred vision.**

Good Luck 😊