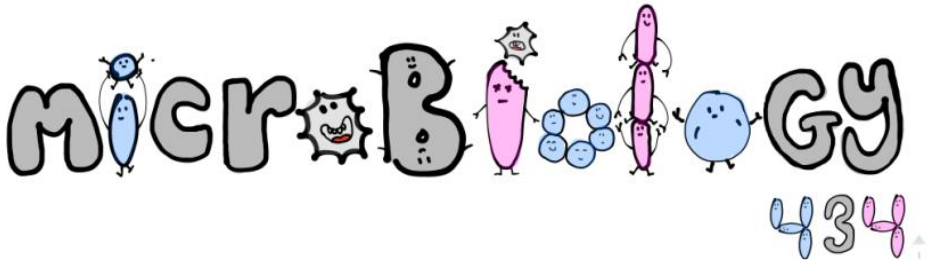
Normal flora & Diarrhea



Introduction to Normal Flora:

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

Normal Flora of The GIT:

- The oral cavity: contain **very high number** which varies from site to site of the mouth.
- Saliva: contain mixed flora **10x8** organism /ml.
- Stomach: **very few** in health due to HCL and peptic enzymes.
- Small intestine: very **scanty** except near colon.
- Colon of adults: **10x 10** org/gm stool
    - >90% are *Bacteriodes* (anaerobic)
    - 10 % other bacteria.
- Direct effect of diet composition.

Normal Flora of GIT:	Normal flora (low virulence)	Potential pathogen (carrier)
Mouth:	Viridans streptococci, *Neisseria* spp., *Moraxella, Peptostreptococcus*.	*Candida albicans*.
Nasopharynx:	*Niesseria* spp., Viridans sterpt. *Moraxella, Peptostreptococcus*.	*S.pneumoniae, N.meningitidis, H.infuenzae,S.pyogenes, S.aureus.*
Stomach:	Streptococci, *Peptosterptococcus*, others from mouth.	None.
Small intestine:	Scanty, variable.	None.
Colon of adults:	*Bacteriodes, Fusobacterium, Bifidobacteria, Lactobacillus,* enterobacteria, *Clostridium*.	*B.fragilis, E.coli, Pesudomonas, Candida, Clostridium.*
Colon of Breastfeeding infants:	*Bifidobacterium, Lactobacillus.*	None.

Role Of GIT Normal Flora In Disease:

- Many are opportunistic pathogens
    - E.g. **perforation of the colon from ruptured diverticulum,** feces enters into peritoneal cavity and cause peritonitis.
- *Viridans* strept. of oral cavity enters blood and colonize damaged heart valves.
- Mouth flora play a role in dental caries.
- Compromised defense systems increase the opportunity for invasion.
- Death after lethal dose of radiation due to massive invasion of normal flora.

Role of Normal Flora In Diarrheal Diseases:

- *E.coli* is the most common Enterobacteriacae , a facultative flora of colon followed by **Klebsiella, Proteus and Enterobacteria**.
- **Salmonella, Shigella** and *Yersinia* are NOT a normal flora of the intestinal tract.
- Some strains of **E.coli ,Salmonella ,Shigella and Yersinia enterocolitica** are able to cause diseases in the intestinal tract. Found in small amounts

Intestinal Pathogens:

- **Invasive and cytotoxic strains** produce inflammatory diarrhea (Dysentery) with **WBCs** and /or **blood** in the stool.
- **Enterotoxin –producing strains** cause **watery** diarrhea with loss of fluid.
- Some produce **systemic illness** due to spread to multiple organs such as **enteric (typhoid) fever**.

Acute Diarrheal Illnesses And Food Poisoning:

Background:

- Acute diarrheal illness is one of **the most common** problems evaluated by clinicians.
- A major cause of morbidity and mortality worldwide.
- Most of healthy people have mild illness but others might develop serious squeals so it is important to identify those individuals who require early treatment.

Definitions of Diarrhea:

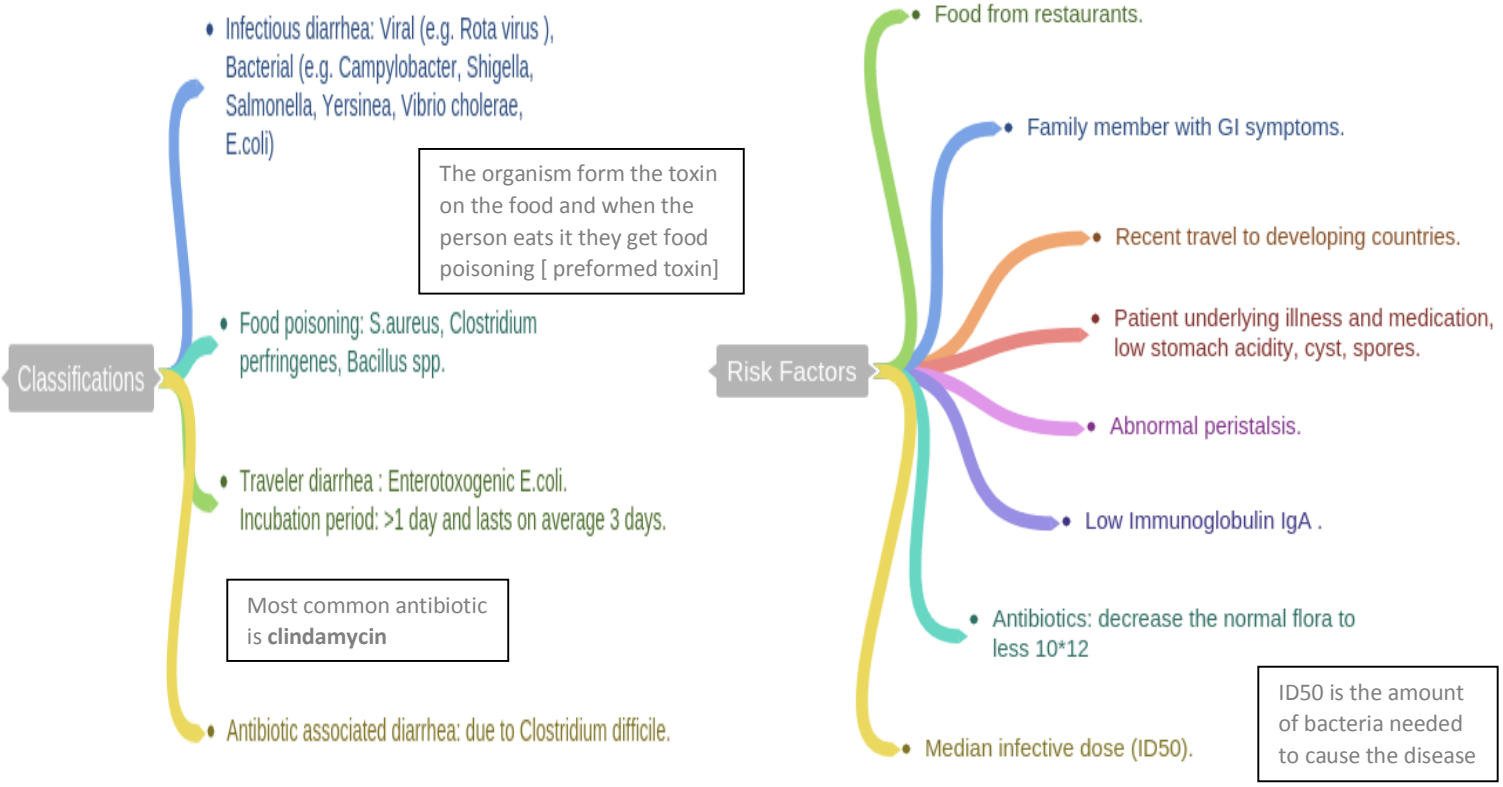
- Stool weight in excess of 200 gm/day.
- Three or more loose or watery stools/day.
- Alteration in normal bowel movement characterized by decreased consistency and increased frequency.
- Less than 14 days in duration.

Etiology:

- **Viral**: **70-80%** of infectious diarrhea in developed countries.
- **Bacterial**: **10-20%** of infectious diarrhea but responsible for **most cases of severe** diarrhea.
- **Protozoan**: less than **10%.**

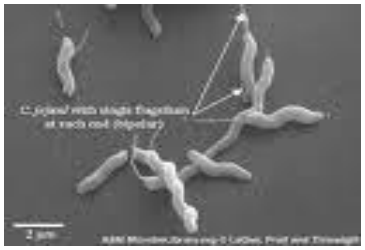
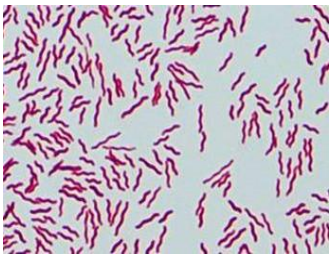
Epidemiology:

- 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 in daycare.
- Seasonal peak in the winter.



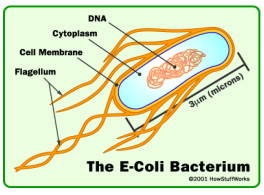
Clinical Presentation and Pathogenic:	
Mechanism I **Enterotoxin mediated** **[non inflammatory]**	**Mechanism II** **Invasive** **[inflammatory]**
Lack of pus in the stool (no gut invasion)	**Pus and blood** in the stool
Lack of fever	**Fever** due to inflammation
Rapid onset of preformed toxin : <12 hrs	Incubation period 1-3 days [shorter]
Small intestine affected	Affect **colonic mucosal surface** of the bowel
Vomiting ,**non-bloody** diarrhea, abdominal cramps.	Dysentery syndrome- **gross blood and mucous** **EHEC** [enterohemorhagic E.coli] **bloody** diarrhea
Vibreo cholerae, Staphylococcus aureus, Clostridium perfringens and Bacillus cereus **[toxin forming]**	**Shigella, Salmonella spp., Campylobacter, some E.coli and Entameoba histolytica**
Other viral and some parasitic infections.	**Entameoba histolytica** 1-3 wk
-	Extension to lymph nodes

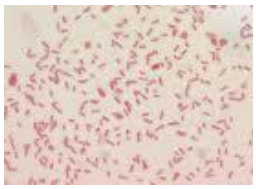
Campylobacter

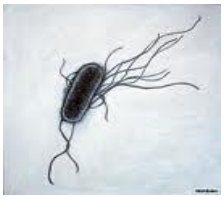
Family	Campylobacteraceae.
Genus	Archobacter-spiral shape.
Common species	**C.** jejuni, **C.** coli, **C** fetus.
Source	Dog , cat, birds, **poultry** ,water, milk, meat, person to person transmission can occur.
Pictures	 [blood agar w/ antibiotics to inhibit other non pathogenic bacterial growth]   spiral shape
Clinically	**Incubation period:** 2- 6 days Take a stool sample [stool is full of bacteria that's why we look for pathogens there] Abdominal cramps – **bloody** diahrea – nausea and vomiting are **rare** Self limiting after 2 – 6 days Chronic carrier Guailian barrie syndrom and reactive arthritis may result
Laboratory diagnosis	**Transport media: Cary blair** **Campybap** [blood agar] contain antibiotics Incubate in [5% O2 – 10% CO2 – 85% N – 42 C except C.fetus 37 C] We mostly look for the most common organisms [dhigilla – salmonella – cambylobacter] The most common virus seen I the lab is [Rotaa virus]
Treatment	**Resistance to CIPROFLOXACIN** **Sensetive to ERYTHROMYCIN – TETRACYCLIN**

E.coli:

- Only about **10 -15%** strains of *E. coli* strains are associated with diarrhea.
- Based on virulence factors, clinical manifestation, epidemiology and different **O** and **H** serotypes.







- There are **Five** major categories of diarrheagenic *E.coli*:
  1. **Enterotoxigenic E.coli (ETEC)**
  2. **Enteroinvasive *E.coli* (EIEC)**
  3. **Enterohemorrhagic E.coli (EHEC)**
  4. **Enteroadherent *E.coli* (EAEC)**
  5. **Enteropathogenic *E.coli* (EPEC)**

Enterotoxic E.coli (ETEC)

- Major cause of **traveler's** diarrhea in **infant and adult** in developing countries from **contaminated food and water**
- **It has high infective dose 10^6-10^{10}**
- Produce:
  - **heat-labile toxin** (LT) leads to accumulation of C-GMP, which lead to hypersecretion.
  - **heat-stable toxin** (ST)

  each has two fragment (A and B)

  A → Active part / B → Binding part
- **Symptoms** :watery diarrhea, abdominal cramps and sometimes vomiting
- No routine diagnostic method. [self limiting – Hx of travel could be a key for diagnosis]

Enteroinvasive *E.coli* (EIEC)

- Produce **dysentery (penetration, invasion and distraction)**
- Similar to ***Shigella* spp**. **(non motile, non-lactose fermenter)**
- **Fecal -oral route**
- Fever, severe abdominal cramps, malaise and watery diarrhea
- Infective dose = 10^6
- Diagnosis : **Sereny test** and **DNA probes.**

❖ Sereny test:

[incubation of the bacteria into an animals eye]

Enteropathogenic *E.coli* (EPEC)

- **Infantile** diarrhea
- Cause **outbreak** in hospital nurseries and day care centers.
- Low grade fever, malaise, vomiting and diarrhea.
- **Mucous** in stool but **no blood.**

Enteroadherent E.coli (EAEC)

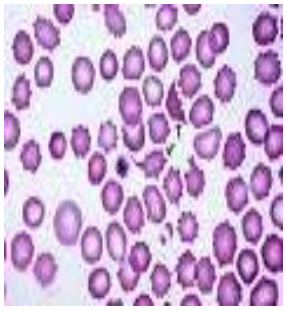
- **Pediatric** diarrheal disease
- **Adhering** to the surface of the intestinal mucosa ,can **cause UTI.**
- Aggregative stacked brick in the mucosa
- Watery diarrhea, vomiting, dehydration and abdominal pain for two or more weeks

Enterohemorrhagic E.coli (EHEC)

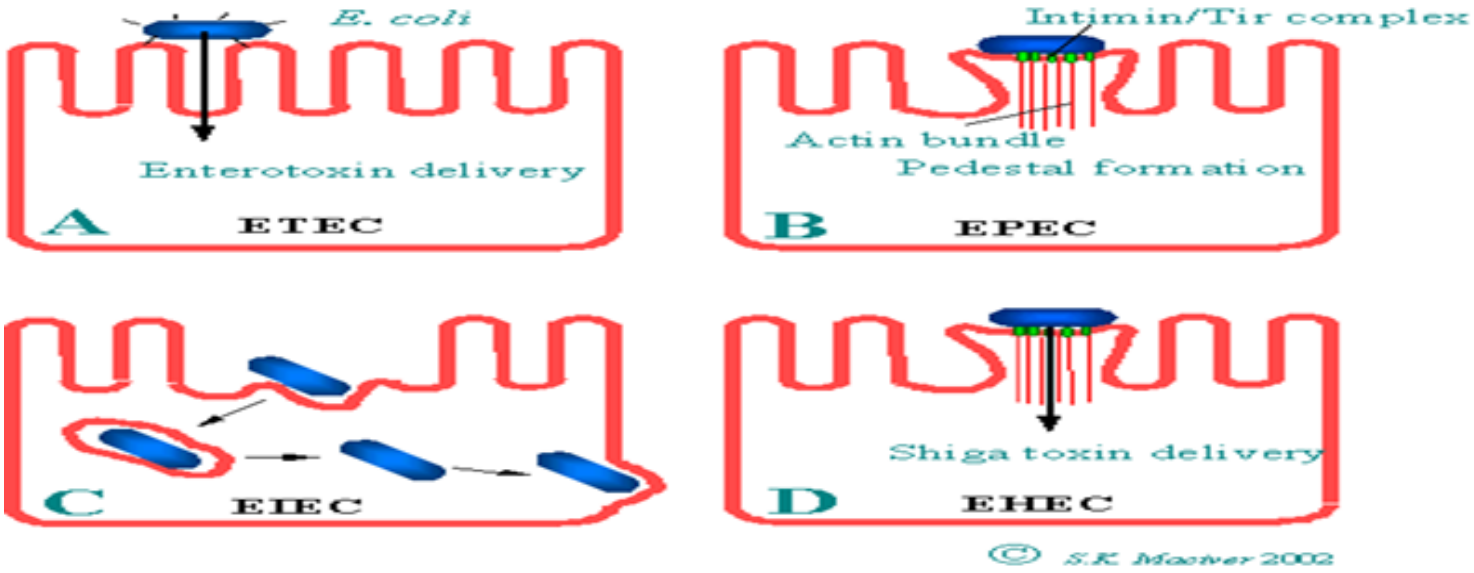
- **O157:H7 :**
  - Hemorrhagic diarrhea
  - Colitis
  - hemolytic uremic syndrome (**HUS**):

[low Platelet count, hemolytic anemia and kidney failure]

- **Bloody** diarrhea, low grade **fever** and stool has **no leucocytes**
- **Fatal** disease in young and elderly persons in nursing homes
- Transmitted through consumption of:
  - undercooked hamburgers
  - unpasteurized dairy products
  - apple cider
  - cookie dough
- **Cytotoxin = Vertoxin I and Vertoxin II similar to (Shiga-toxin I &II)**
- *E.coli* other than **O157:H7** can cause **HUS**
- Diagnosis by culture on **SMAC***(sorbitol MacConkey agar cefixime*), Vertoxin detection by **immunological test** or **PCR.**
- **HUS:** Hamburger disease



Distruction of RBCs + low PLTs



A: produces the toxin and injects it inside the cell
B: Pedestal formation [أقدام كاذبة] and destroys the mucosa
C: most serious one because it invades – destroys – spread to other cells
D: Forms toxin – Destroy the cell

Yersinia enterocolitica:

- Mesenteric lymphadenitis → children
- septicemia → immunocompromized hosts
- Common in Europe, USA, Canada . Cats, dogs & swine (chitterlings)
- Survive **cold temperatures** and associated with transfusion of packed red blood cells.
- **Present with enteritis, arthritis and erythema nodosum** [not all of them are GIT symptoms]
- Generalize infection in adult and children 1-5 yrs, usually mild but in old children and adult it **mimic appendicitis**
- Grow at **25°-30°C .**
- **Media:** Cefsulodin-Igrasan-Novobiocin.

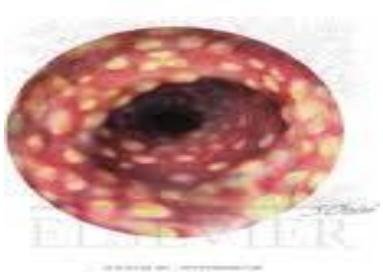
Clostridium difficile:

Antibiotic associated diarrhea: [Clindamycin]

- 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
- Produce **toxin A and B** that can bind to surface epithelial cell receptors leading to inflammation, mucosal injury and diarrhea.
- Patient presents with **fever, leukocytosis, abdominal pain and diarrhea**
- **Pseudomembrane (consists of 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

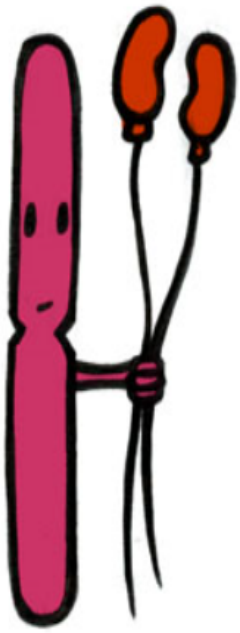
Spores

Endoscopy: Pus cells w/ severe inflammation



Blood agar

Selected Clinical and Epidemiologic Characteristics of Typical Illness Caused By Common Foodborne Pathogens*				
Pathogen	**Typical Incubation Period**	**Duration**	**Typical Clinical Presentation**	**Assorted Foods**
Bacterial				
***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.



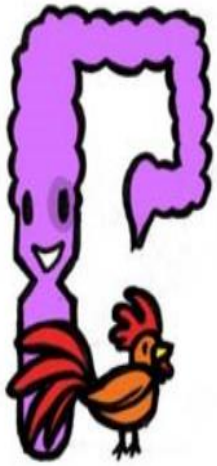
ESCHERICHIA COLI

Hey, my name is E. coli.
I'm a Gram negative bacteria and I'm part of the enterbacteriaceae family.
In my family I am part of tribe I, Escherichieae.
My whole family is oxidase negative.
I live in the bowels.

My uropathic strains are the most common cause of urinary tract infection. For teh win!
Some of my strains have virulence factors, so I can cause diarrhoea.
The diarrhoea can watery or bloody, depending on which strain you have.

Hola. I'm C. jejuni.
I am a curved Gram Negative rod.

You can find me in lots of domestic animals.
I am part of the normal bacterial flora of poultry and cattle.
I get into people through dirty drinking water or undercooked meat, especialy chicken.
I cause food poisoning, with a self limiting bloody diarrhoea, abdominal cramps and fever.



CAMPYLOBACTER JEJUNI

Hey there, my, name is Y. enterocolitica.
I'm Gram negative, an Enterobacteriacea bacteria.
I'm part of the tribe Yersiniae.

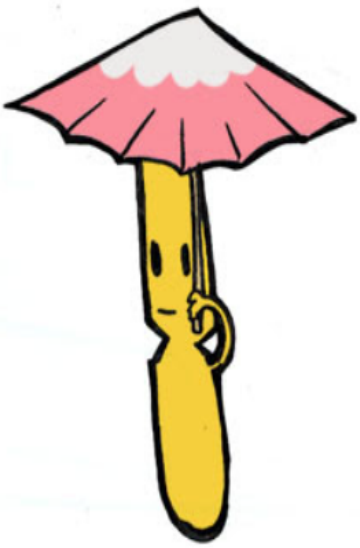
I'm not as well known as my cousin Y. pestis, but I'm still important.
I get to you in food and I love pork.
I can cause abdominal pain and diarrhoea.
Kids are my favourite.

But look out! when I infect your lymph nodes and your ileum, I can look just like appendicitis.

YERSINIA ENTEROCOLITICA

Hello, my name is C. difficile.
I'm an anaerobic, Gram Positive rod that can make spores.
I live in your digestive tract.

I cause pseudomembranous colitis.
Sometimes if you take broad spectrum antibiotics (especially clindamycin and the cephalosporins) you kill off your friendly bacteria.
That leaves lots of room for me.
I make toxins that cause very bad inflammation.
You get diarrhoea, abdominal pain and a fever.



CLOSTRIDIUM DIFFICILE

I covered myself in a white membrane like coating that can be seen on the inside of your intestines.

MCQs:

1-A patient was hospitalized after an automobile accident. The wounds became infected and the patient was treated with Tobramycin, Carbenicillin, and Clindamycin. Five days after antibiotic therapy was initiated the patient developed severe diarrhea and pseudomembranous enterocolitis. Antibiotic-associated diarrhea and the more serious pseudomembranous enterocolitis can be caused by:

A- Clostridium sordelli B-Clostridium perfringens C-Clostridium difficile D-Staphylococcus aureus

2-A box of ham sandwiches with mayonnaise prepared by a person with a boil on his neck was left out of the refrigerator for the on call interns. Three doctors became violently ill approximately 2 h after eating the sandwiches. The most likely cause is:

A- Staphylococcus aureus enterotoxin B-Coagulase from Staphylococcus aureus in the ham

C-Staphylococcus aureus leukocidin D-Clostidium perfringens toxin

3-Symptoms of Clostridium botulinum food poisoning include double vision, inability to speak, and respiratory paralysis. These symptoms are consistent with:

A-Invasion of the gut epithelium by C.botulinum B-Secretion of an enterotoxin

C-Endotoxin shock D-Ingestion of a neurotoxin

4-The treatment of choice for a patient with Campylobacter jejuni enterocolitis is:

A-Erythromycin B-Ciprofloxacin C-Ampicillin D-Pepto-Bismol

5-A 2-year-old infant was brought to the emergency room with hemolytic uremic syndrome and thrombocytopenia. Which of the following bacteria would most likely be isolated from a stool specimen?

A-Shigella B-Salmonella C-Aeromonas D-Escherichia coli 0157/H7

6-E. coli causes disease by a variety of different methods. Which one of the following E. coli types is characterized by the presence of LT (heat-labile) and ST (heat-stable) proteins?

A-Enteroinvasive (EIEC) B-Enterotoxigenic(ETEC) C-Enterohemorrhagic(EHEC) D-Enteropathgenic(EPEC)

7-For each of the following body sites, choose that bacterium that is the predominant normal flora (indigenous organism)

A-Alpha-Hemolytic streptococci	1-Skin
B-Lactobacillus	2-Mouth
C-Staphylococcus epidermis	3-Bowel
D-Escherichia coli	4-Vagina
E-Bacteroides fragilis	

ANSWERS:

1- C 2- A 3- D 4- A 5- D 6 - B 7- SKIN (C) , MOUTH (A) , BOWEL (E) , VAGINA (B)

Good luck .. <3

حنان محمد عبدالمنعم

ملاك الخثلان

رنا براك

أشواق المطيري

رشا بصاص

حنان خشيم