

Digestive System

University of Jordan
Faculty of Medicine
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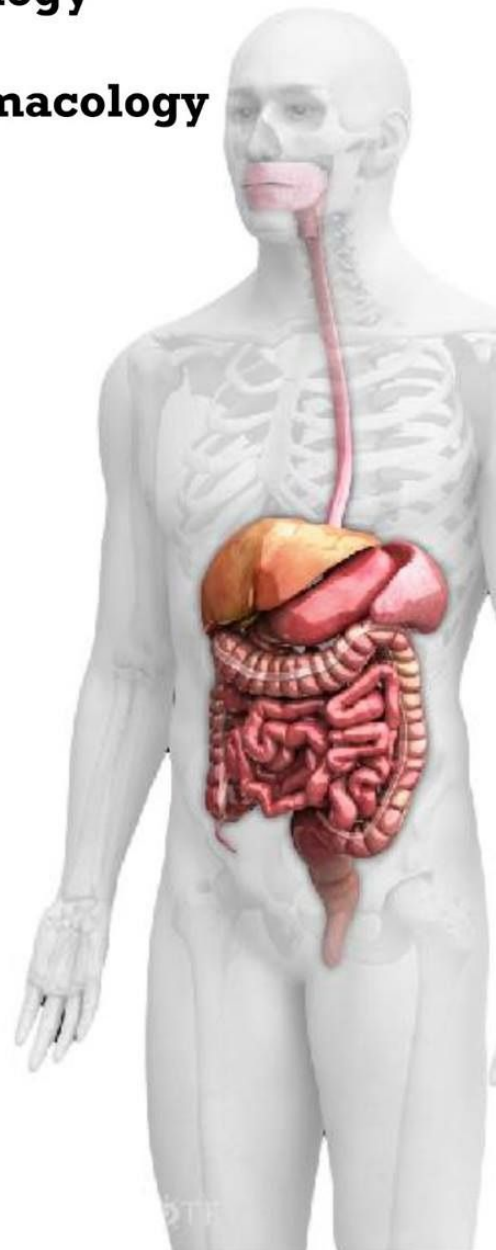


Slide Sheet Handout Other

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Sheet #: 2 (Bacteriology)
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Date:
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Diarrheagic E.coli and others ..

We've already mentioned 1st group which called **enterotoxigenic E.coli** which is widely distributed in the Intestinal Tract of human and animals and often associated With contaminated food and water, causing mainly Diarrhea in young children (watery Diarrhea) rarely associated With contagious and often self-limited.

Generally, any person infected with these enterotoxigenic E.Coli develops immune response especially in relation to intestines which experience reoccurrence of this organism.

Whereas more dangerous and more associated with contamination which called **Entero-hemorrhagic E.coli**. Which are associated with release of toxins known as **shiga toxin** or **viro toxin** in relation to tissue from types of cells which means produce more damage in Intestinal Tract due to release these shiga-like toxin.

The problem with these toxins, that it might be absorbed later and associated with complications, like hemolytic uremic syndrome (HUS).

There are many serotypes associated with this organism, but the most important one is **0157:H7** in relation to somatic Ag and O Ag , this type of enterohemolytic E.coli is found mainly in large animals' Intestines like cows and camels and other types, and it transmitted to human by close contact or contamination of meats especially raw meats in producing large amount during preparation like Hamburger.

Might be associated with outbreaks of gastroenteritis which involve 100-1000 infected people. If sufficient amount of toxin is produced and

reaches Blood stream and carried to kidney, clinical syndrome will be HUS which means damage of kidney, released of blood and protein in urine and later associated with fatal outcome.

Enteroinvasive E.coli , similar to some extent to shigella , but produces another cytotoxins associated with ulceration in large intestine and Bloody Diarrhea .And mainly associated with other gastrointestinal symptoms like : vomiting .

Normally all Enterohaemorrhagic E.coli require treatment with antibiotics in contrast with other Enterotoxigenic E.coli, to prevent production of sufficient amount of toxins not to reach blood stream.

Enteropathogenic E.coli

Related to lipopolysaccharides of the cell wall, which means it's NOT associated with release of any toxins or cytotoxin or endotoxin, often produce diarrhea in **infants up to age 6 months**. Normally produce mild diarrhea but may associated with chronic diarrhea and death of the child. After other 6 months, generally children produce immune response and often they will be not more susceptible to this type of Enteropathogenic E.coli.

- It's not important in adults, only in children.
- Considering lab diagnosis of all types of Diarrhagenic E.coli, it's not easy to distinguish between commensal E.coli (normally found in our intestines) and these pathogens, therefore culture on macconkey agar and other type of agar can't easily distinguish between pathogenic and not pathogenic ones. The only way is doing biochemical reaction and **stereotyping** . Which is not available in most labs , therefore only way is during PCR , in order to detect the genes responsible for these types of **enterotoxigenic**

E.coli and **entero-pathogenic E.coli** , considering these 2 types often require no treatment, only to control dehydration and to replace fluid loss in infected person . Whereas **entero-invasive** and **entero-hemorrhagic E.coli** should be treated with antimicrobial drugs like ciprofloxacin, and co-trimoxazole in children.

- No vaccine available at all.

Campylobacter

Discovered recently, outbreaks in children in England.

G^{-ve} microaerophilic bacteria, not easily identified in normal culture media, it needs special antibiotic type media → campylobacter media.

It's better to grow it in higher temperature media **more than 37°C (usually at 42°C)**, while other types are usually grown at 37C.

Originated from intestines of domestic and wild animals especially dogs and cats, might contaminate our food especially fresh food → Diarrhea.

Depending on species of campylobacter, there're many types of the diarrhea:

- 1- Campylobacter jejuni: related to small intestine, **Watery Diarrhea** and rarely bloody diarrhea
- 2- Campylobacter fetus: more common, causing more ulceration and **bloody diarrhea**.

Both species might spread to blood stream and cause **blood sepsis**, they are more invasive than shigella and salmonella in producing blood sepsis, especially in immune compression condition and children.

Normally, under health condition, no need to give antibiotic drugs, only control dehydration, if necessary replacing by oral tube without any complication.

Repeated infection of campylobacter might be associated later with other clinical features especially in relation to mild bacteremia, which results in reactive arthritis and other mild complications related to connective tissue. Which are due to repetitive exposing to Antigen of campylobacter.

Treatment : macrolides and azithromycin

In general, in Middle East is less than west, because we rarely have pets (cats, dogs) inside our homes since cats and dogs have Campylobacter normally as their normal flora.

H.pylori

Known as only organism which associated with our mucosal gastrointestinal, especially stomach, recently discovered, at the beginning they didn't consider it as an important organism, cuz there was no proof that this organism is associated with any clinical disease, because children early in their life become colonized with H.pylori and slowly with increasing in age, the % of colonization of this organism increases.

Studies indicate that 90% of world population is colonized with this organism. In our country, there is 60% of young adult colonized with H.pylori, this means H.pylori might colonize our intestine without causing any infection and clinical diseases.

But under stress condition or using certain types of drugs, can be activated and associated with **gastritis**.

This organism is flagellated with no. of long flagella → which manage to attach to mucous of stomach mucosa.

Following attachment by production of potent urease enzyme which will mainly affect presence of proteins in mucosa result in production of CO₂ and ammonium chloride, which will neutralize the action of HCl acidity of stomach and allow the organism to accumulate and produce mild ulceration.

Ulceration might not be recognized clinically without symptoms and pain. May produce damage resulting in duodenal ulcer and gastritis.

Again this organism produces very potent **urease enzyme** → which is responsible to support colonization of this organism in the mucus of the stomach.

Allowing it to penetrate the submucosa and produce ulceration.

Generally, about 1-3% of population who are colonized with H.pylori might develop later symptoms of gastritis and duodenal ulcer, and under certain condition might be associated with gastric lymphoma and gastric adenocarcinoma.

Therefore, it's not easily to control presence of colonization , despite the fact that there are antimicrobial drugs can eradicate 90% of organism from infected sites.

- 100% of eradication is not available.
- Recurrence is always observed later on, after 2 months, and this depends on the general health conditions and stress condition of person.

This organism produces 2 types of toxins:

- VacA (vacuolating toxin)
- CagA toxin (cytotixin)

Both depend on the multiplication of the organism and other factors related to the acidity of the stomach.

If acidity is low, we've to expect more cytotoxigens to be produced and more ulceration.

No vaccine available.

Diagnosis: accomplished by many means:

~ Simple mean to have test known as **urea breathe test** to detect presence of ammonia in oral cavity.

~ Or in stomach by using special capsule.

~ Or to take biopsy from infected site and look for the presence of urease enzyme and to demonstrate the organism in cytological preparation by using **Giemsa stain** and **silver stain**.

- Gram stain can't help, because the organism is not easily demonstrated.
- Culture usually done under optimal condition. (37-42c; like Campylobacter).

Despite the fact that human develop specific Abs against this organism, this should not be taken as *diagnostic test* , because majority of population normally have this level of Abs against this organism, so serological test must be done only if there is increase in Abs level four folds . Otherwise it will not be significant.

Treatment : there are 2-3 antibiotics should given together , like metronidazole and clarithromycin and anti-acids , this combination should be continued at least 4 weeks , eradicated is not 100%.

It's only for short period. Patient will recurrent this infection.

Infection is not easily controlled without controlling the stress condition.

Vibrios

Live in different types of water more than 20 species found in sea water and in any type of body water.

2 species are the most important:

#Classical one : associated with elaboration of **cholera toxins** and from these classical one, we've subspecies which have developed following mutations with this organism.

L2 type of vibrio cholera: which are considered now prevalent type of vibrio in the world.

Classical one → a- in relation to presence of somatic Ag 01

b- presence of other somatic Ag known as 139 .

Both associated with outbreak epidemic of cholera , responsible for at least in each year 1,000,000 cases of cholera disease.

* **Heat labile toxin** , same mechanism as enterotoxins heat labile toxin of E.coli, different in amount of toxins , here it's concentration is 10-100times of other enterotoxigenic E.coli, which means **severe dehydration** which can be within few hours and might end body fluids in less than result in complication, cardiac arrest - kidney failure - death.

- Only way to cure the patient is replace the loss of fluids in short periods (losing 1 L == replacing 1 L), IV fluid patient given. Sufficient amount of fluid during severe dehydration are not given orally because patient will vomit it directly and will not accept any oral fluid. Generally

within short periods, there will be recovery and the organism will produce less amount of toxins and intestine begins to recover normally and produce specific anti-toxin bodies which prevent later the complication with vibrio cholera.

It's not invasive organism, can't reach blood stream, only related to intestines in producing toxins. Antibiotics only will decrease no. of vibrio cholera in intestines and to decrease possibility of transmission of organism from person to other, mostly this organism follow contamination of water, rarely by close contact or food contamination. So measuring hygiene of water is important in prevention water contamination. It always occurs in outbreaks in communities, no sporadic cases.

Normally follow infection with vibrio cholera, infected persons develop intestinal immunity which persist for 1 year, after that the patient may be susceptible to vibrio cholera, so oral vaccine can be given to prevent for short period, not recommended for healthy people.

*other types of vibrio cholera:

#Non-01 vibrio cholera

which produces **watery Diarrhea** , it's to some extent similar to classical type , not so severe.

Not due to release of cholera toxins which responsible to activation of cAMP and release of Na^+ and K^+ etc.

It's more cytotoxic → affect mucosa of large intestines.

It's associated with original type which means due to chromosomal mutation in classical vibrio cholera, there will be loss of gene which responsible for producing cholera toxins.

Vibrio parahemolyticus , is related mainly to fish , this organism considered **invasive** , might produce gastroenteritis , dehydration and watery Diarrhea , might produce sepsis and wound infections .

1st and 2nd types are not associated with invasion .

Lab diagnosis for all these Vibrios is by using same culture media known as: TCBS culture medium (4 components: Thiosulfate-citrate-bile salts-sucrose medium)

Which recognize **yellow color** of the organism and this medium inhibits growth of other intestinal flora and later we do biochemical test and serotyping confirmation with specific antisera to differentiate different subtypes.

prevention : only way to have safe water and control fresh drinks especially in outdoor and during sport activities , in order to have less contamination with these organisms .

healthy carrier in cholera : a person who might carry the organism for short period -not more than 3 weeks- and without any clinical symptoms , infections with vibrio cholera not necessary associated with watery Diarrhea and clinical cases , normally 30% of persons who infected by classical or non-classical , develop clinical feature of vibrio cholera , other 70% might develop mild diarrhea or develop nothing , so 70% are considered asymptomatic .

Now in short:

Food poisoning organisms , are not important only in presence of bacteria in intestinal tract , it's more important in release of toxins in already presented food , which means if there is contamination of food particles with these types of bacteria , you should expect that these

organisms will release potent toxins → responsible for food poisoning or what we called food intoxication .

Clinical feature due to presence of toxin in the food not due to presence of bacteria in the intestine like vibrio cholera or other types.

***Heat stable toxins** (not easily being inactivated by boiling temperature up to 20 minutes).

Associated with cases of food poisoning, manifested firstly with vomiting then later may be associated with watery Diarrhea .

Often intoxication with **S.aureus** is self-limited , without any complications , and patient will recover within short periods without complications, so no need to get antibiotics since we're dealing with toxins only.

There are cases especially in immune compromised patients, might S.aureus reach in high no. in intestines and might associated with gastritis but very rare .

Bacillus cereus (aerobic) produces 2 types of toxins :

- 1) Outside the body, known as **emetic enterotoxin** responsible for foods intoxication and poisoning, without multiplication of the organism inside the intestine, clinical features is similar to S.aureus, can't distinguish clinically between staph and bacillus cereus.
- 2) Bacillus cereus , if ingested in huge no. , might produce toxin known as **diarrhegeric toxin** , normally released within presence of bacillus cereus inside the Intestine in contrast to other types of toxins , and this might be associated with watery Diarrhea.

- In both cases *Staphylococcus* and *Bacillus cereus* → no fever, which easily can be recognized for differential diagnosis.

Another form of bacteria called ***Clostridium perfringens*** (spore forming anaerobic) , produces 2 types of toxins :

- 1) outside -toxin type A, responsible for vomiting , less diarrhea without fever.
- 2) inside –toxin type C, responsible for watery Diarrhea , and might produce Bloody Diarrhea and more complications .

Anaerobic - spore forming, not easily be killed by boiling temperature.

*Rarely might reach Blood stream and produce sepsis .

*Mainly associated with type A and very rare type C.

Concerning ***Clostridium botulinum*** is highly potent toxin → normally performed outside the body in canned food (beans, fish..) In relation to amount of toxin; which less than one microgram can be enough to kill the person within 3 hs , most potent toxin !

Heat -stable (can't be killed by boiling for 20-30 mins) once absorbed can't be easily to treat patient (toxin will be absorbed in the nerve endings of CNS) and inhibit Ach release and produce **paralysis** in relation to respiratory tract or heart and other organs resulting in Death.

2 other organisms:

- 1) ***Yersinia enterocolitica*** , in intestines of domestic animals especially pigs and dogs , contaminated food (diary products), more common in west countries , Diarrhea.

***invasive** lead to blood sepsis , complication especially in immunocompromised patient (ICP) and gastric infection .

2) **aeromonas and pseudomembranous** , might produce some cytotoxin and diarrhea in young children and ICP , rarely associated with complications.

Lastly , **Clostridium difficile** , spore forming bacteria , part of normal intestinal flora and at least 30% of population is colonized with this organism.

During treatment with certain types of antibiotic , this organism might increase in no. in intestinal tract and release very potent cytotoxins which produce severe irritation and ulceration in the colon following that producing pseudomembranous colitis → might be 1st mild , not recognized but later it might associated with outpouring of blood from intestines causing severe damage to the colon and eventually death.

This diarrhea is known as Antibiotic associated enterocolitis.

Clindamycin enhance replication of C.difficile

Treatment : stop use potential causative antibiotics, and use metronidazole / vancomycin instead.

The End ..

إن كان سمحتوا يا شباب وصبايا تسامحونا وتدعولنا

موفقين ☺

Even though I believe no one will reach this point except the corrector :')