

***Sheet no. : 19***

***Refer to slide no. : 11 , 12***

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Our lecture today is about another type of **enterobacteriacae**, which is salmonella.

We talked before about other salmonella that come from birds and animals and will cause diarrhea (salmonellosis) and enteric fever.

We have a type of salmonella which is called salmonella typhi that causes a serious disease, also another type called paratyphi (A,B,C) causes the same disease but it's less severe than the one caused by typhi.

**Enteric fever = typhoid fever** حمى التفؤيد

- are found only in humans (not in animals).

- transmitted between human beings through fecal contamination. when a carrier went to a toilet, then he didn't wash his hands and went to cook, then the disease will be transmitted from the carrier.

- found in food and also in water, but usually in food.

- Incubation period is between 10 days to 2 weeks.

- bacteria invade epithelium of G.I.T and go through regional lymph nodes, then multiply there to go to the blood and produce septicemia-bacteremia that spreads from infected organs to the liver, spleen, lymph nodes, and bone marrow. there, it will also multiply.

- These are the initial targets of inflammation/infection by these organisms.

- You get some sorts of signs and symptoms:

 -fever -PUO pyrexia of unknown origin

 -constipation -malaise

 -headache

 -fever goes up and down.

 These are the initial symptoms of typhoid fever, but they are difficult to designate to typhoid fever (means that these signs are shared between lots of diseases not only for typhoid fever).

- After multiplying in the regional lymph nodes, they go back to blood and produce a second septicemia, then migrate to G.I.T and gall bladder, and also multiply and make infection to G.I.T, to produce diarrhea (which accompanies typhoid fever), moreover, they make necrosis to some areas of the G.I.T especially Peyer's Patches.

- Typhoid fever is a really serious disease, unless treated, it will cause death.

- has mortality of 50% , or maybe more.

- lucky to not have it nowadays, but it was present before.

- It's difficult to diagnose.

- During **1st week**, it's really difficult to be diagnosed, we rely on taking **blood** culture from the patient and isolate it.

- After **2nd week**, patient will have diarrhea, so we rely on **stools**.

- **3rd week**, it will appear in the **urine**.

- as conclusion, it firstly appear in blood, then in stool, finally in urine.

- we can also use serology as Widal test, look for antibodies in the serum against salmonella typhoid antigens, it's an agglutination reaction, we used to demonstrate a rising titers of serology (if we take patients serum, and check for these antibodies using agglutination, after 1 week, if there is rising in antibodies count, means salmonella typhoid is present, and the patient is infected- because of the immune response is rising) .

- as we said, septicemia actually occurs.

- by infection of typhoid, its important and serious in young and old people, because of that the immune system is compromised(not working well).

- it's said to be that if you treated or not, some people recover by their own.

- unfortunately, some cases become carriers- in spite of treatment-or become chronic carriers, those are: -asymptomatic, but they still can pass the infection to other people by their feces, if they handle food or water after.

- **Gall bladder** is a reservoir of salmonella typhoid, so people who are chronic carriers will have chronically infected organs, like the gall bladder , so its responsible for secreting bacterial-typhoid toxin in feces, but these patients are normal, not suffering from the disease , and are asymptomatic (toxin is not presented in their blood, but in their feces, so they can pass the infection to others by food or water).

- Salmonellosis (zoonotic) , comes from birds and animals.

- Salmonella typhi and paratyphi, the human is the only reservoir for them (the only host).

- Recall, the reservoir of typhoid is the gall bladder.

- when treating chronic carriers by antibiotics, because you need to eradicate the bacteria, and sometimes you need to remove the gall bladder (reservoir) to protect other people.

- how to know the carriers----[check the **feces**].

- There was a TV series called Typhoid Marie, she is a house cooker, that migrated from Europe to America, and every place she went, she transmitted the disease when she cooked, after discovery, they isolate her in a hospital till she died.

- The way of transmitting infection is **FECO-ORAL.** contaminated hands with bacterial-toxin, then touch food, then people eat the food and get infected.

-recall, chronic carries who aren't cured completely, their gall bladders secrete typhoid toxin in feces.

-There is a vaccine against typhoid, taken in skin, intramuscular, and orally.

- It's good to take the vaccine if you are going to an area which is infected, other than that, it's not a routine vaccine like the triple vaccine.

Now we are going to talk about  **Shigella**

- Shigella is an Enterobacteriacae.

- confined to human beings (the only host- it's not presented in animals).

- Its pathogenic.

It's very infectious, we need only small amount of bacteria to get infected, e.g:100 bacteria are enough to pass infection.

- needs very close contact(it can't live long outside body), also bad hygiene to be transmitted (spread very quickly between children -no good hygiene\_.

- In areas of crowding, (camps-institutions-foamy places),shigella spreads easily.

- The way of transition is **also FECO-ORAL**.

- Incubation period is short (1-3 days).

Signs and symptoms:

 - Usually watery diarrhea as a **first stage**(a result of small intestine infection by shigella)

 - Then bacteria will move to large intestines and attack cells of lining epithelia of large intestines, then produce the shiga toxin (entereotoxin) + the enterocellular survival of these organisms in these epithelial cells, would produce damage.

 - Shigella do not invade any further, they only stay confined to epithelial cells, do not move to blood, hence do not produce septicemia. (unlike typhi).

 - **2nd stage** of disease occurs due to invasion of lining epithelia of large intestines, infection in these areas produces dysentery (frequency of defecation but the amount each time is small, and the stool contains large amount of mucus +blood+ puss, with small amount of feces, characterized by very foul smell.) which is different than diarrhea.

- 2 types of dysentery: - bacillary dysentery caused by shigella

 - amoebic dysentery caused by parasites.

- So, 1st stage of shigella infection is watery diarrhea, the 2nd is invasion of large intestines and dysentery.

Pathogenesis and virulence factors of shigella:

- invasiveness (attachment)

- exotoxin (shigella toxin)

- intracellular survival

- multiplication.

- Shigella invade to attach M cells (in small intestines, work in immune system, phagocytes antigens like parasites).

Characteristics of shigella toxin:

- enterotoxin, neurotoxin, and cytotoxin.

- encoded by chromosomal genes.

- 2 domains (A-5B) structure. most of toxins are of 2 varieties (components).

- similar to shiga-like toxin of enterohemorrhagic E.coli (EHEC), both produce bloody diarrhea, fever, malaise, but shiga toxin doesn't cause renal failure, neither hemolytic syndrome, while shiga-like toxin does.

- Compositions of shiga toxin: - A subunit produces the damage

 - B subunit binds the membrane to enter the

 cell.

-There is no vaccine against shigella.

- Shigella can be fatal, but also it can be cured.

- people can be carriers of shigella (pass infection to others).

We have talked about 3 Enteroobacteriacae : E.coli, salmonella, shigella. the 4th is yersenia.

**Yersenia**

**Yersenia pestis**: the causative agent of the plague "black death".

Plague is a zoonosis: a disease that affect animals, but can spread to human beings……. so plague is a disease of animals mainly rodents, some wild animals and some mammals as camels.

Plague had eradicate half of the European in the 16th century.

Plague occur in two varieties:

1. Urban plague: comes to people from rats that live in cities, these rats are usually infected by plague.

The disease spread from one rat to another by fleas. "the vector of the spread of this disease is the fleas"

If you have suddenly drop in the number of the rats because of plague, the fleas need to be feed, but they can't find enough rats, so they attack human beings by biting them then transmit the disease to them.

Manifestations that you find it in the people:

1. Septicemia
2. Enlarging of the lymph nodes especially in the armpit (axillary) & groin (inguinal), so it become like clumps full of bacteria that are buboes. "buboes: swelling of the lymph nodes" ……… so this type of plague is known as **bubonic plague**.
3. The skin will get henry disease and will looks black.

It's not only confined to the lymph nodes, but it can spread to all of the body and attack the lungs, so it will produce pneumonia ………. **pneumonic plague**.

If you develop pneumonic plague then you can spread it to another people by coughing.

(rats people) by fleas

(people have pneumonic plague normal people) by coughing

Person to person transmission in pneumonic plague.

Urban plague is maintained in rat populations and spread among rats by infected fleas. Humans are accidentally infected.

It has been controlled.

1. Sylvatic plague

It still present in the world.

It comes from wild animals (rabbits, rats, mice, prairie dogs).

The vector is the fleas.

You can be infected by eating the meat of this animals (as camels meats) or by handling the contaminated animals.

Person to person transmission is pneumonic plague.

It's zoonosis.

- Pandemic: universal spread of the disease ( in all of the world "spread from one place to another").

- Endemic: the disease found in certain area and even now or then the people will be infected of it.

- Epidemic: sudden explosion of the disease within certain area (ex.: an epidemic of influenza in Amman which will affect most of the people)

🡪Slide 40 (read only)

- The action of the fleas when it takes the organisms:

The organism multiply within the gut of the fleas so it block the gastro intestine tract (here the fleas can't drink the blood of the humans... so it's hungry), then it will regurgitate the organisms in the person that they are biting so they spread the disease. But here it will remain hungry because it can't acquire enough blood into their gut because it's blocked by bacteria.

 (refer to slide 41)

**Yersenia enterocolitica:**

It can cause colitis and diarrhea.

Sometimes it can spread to the blood contamination transfusion leading to septicemia.

**Klebsiella pneumonia**

* Member of the Enterobacteriaceae.
* A special characteristic of it: it have a very nice and marked capsule.
* lactose**-**fermenter (same as Escherichia coli).
* Can be carried as part of the normal flora.
* The main disease that cause by it is: pneumonia.....hospital acquired infection.
* It's appear very mucoid when it grow in Petri dish, because of its prominent capsule.
* It can cause urinary tract infection and septicemia especially in hospitalized and immunocompromised people.

**Proteus**

* Non-lactose fermenter.
* Very motile, because it have many flagella and you get swarming on the media.
* It produce urease (urease break down urea producing ammonia)...... so it's a very common cause for urinary tract infection.

Here the urine will have fishy smell (because the urine contain urea that is broken by Proteus and this produce ammonia that have fishy smell).

**Pseudomonas and Related Nonfermenters**

- Gram negative bacilli

🡪 We will only talk about Pseudomonas

**Pseudomonas**

* Very ubiquitous organisms (present everywhere "water, taps, kitchen sinks and especially in the hospitals" ).
* They may be associated with the normal flora of hospitalized and immunocompromised people, so normal people don't really suffer from Pseudomonas although it's very widely spread and they have lots of pathogens factors, but it is surprising they don't cause lots of infections in normal people.
* They don't depend a lot on nutrition , they can survive on water and little bit of traces elements ..... they don't need special needs like chocolate agar or blood rich agar, they grow very easily on anything, even some of them can grow in disinfectants ( they are really very resistant).
* They are resistance to many antibiotics ..... this a problem ..... but luckily they don't cause much more diseases (just opportunistic pathogens).
* Gram negative, motile (one polar flagella), non- fermenter, and they are oxidase positive.

[Enterobacteriaceae are oxidase negative.... so we can use oxidase test to differentiate between Enterobacteriaceae and Pseudomonas nonfermenters].

* Some of them are very mucoid, so when you grow them you will find that the growth is very sticky and mucoid. Many of the strains produce pigments, so sometimes we find the agar look green, red, black, blue , according to the pigments which produced by bacterial pseudomonas species or strains.
* Some of strains smells like grapes or putrefactive apple sweet stinky smell.
* Pseudomonas have a lot of pathogenicity factors, but it's surprising that it's not cause much more diseases.
* Pathogenicity factor:
1. Produce enzymes
2. Produce toxins
3. They have polysaccharide capsule
4. Pill
5. Endotoxins

 🡪 Slide 9, 10 (know the pathogenicity factors without knowing what they do)

* Clinical Syndromes of Pseudomonas aeruginosa (usually associated with immunocompromised and hospitalized people):
1. Bactermia and septicemia
2. Urinary tract infection , it's very difficult to treat.
3. Pulmonary infections, especially with people have cystic fibrosis (some problems in surfactant of the lungs , genetically inherited recessive disease, not common here but common in Europe).
4. Ear infection, either in the otitis external "inflammation on the external ear" or sometimes it can spread to the middle ear produce "chronic otitis media".
5. It make problems in burn units it cause burn infections.
6. Ecthyma gangrenosum, it radiate as an inflammatory lesion occur in the skin and becomes necrotic. It can be associated with any infection due to pseudomonas , it goes in the skin and make a lesion like a rash and then it became gatherers due to phospholipase.
7. Others: UTI, eye infections, CNS infections, GI infection.

🡪Slide 13 "Burkholderia" (not included)

🡪Slide 14 "Stenotrophomons Maltophilia" (not included)

🡪Slide 15 "Acinetobacter" (not included)