

***Sheet no. : 18***

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

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**Slides 2-3:**

We started talking about *Enterobacteriaceae* , we said that these are gram –ve bacteria, very commonly encountered in medical practice, they are widespread and present in the normal flora of GIT in humans , animals , they might be also present in water and soil ,so they are really very very common. We also said that we have many many genera , many species , but we're going to talk about only 6 of them:

**Slides 4-5:**

*Eschirichia Coli, Shigella , Salmonella , Yersinia ,Klebsiella* and *Proteus.*

These previous mentioned , when are present in the human body , that means that they will cause disease these are called "**True pathogens**", e.g *Salmonella* *,Shigella,* and SOME *E.coli* " enterohemorrhagic *E.coli* is an example (that will cause a disease)". While *Klebsiella* and *Proteus* and SOME other *E.coli*  they can be present as normal flora but sometimes they can cause disease , so we call them "**Opportunistic pathogens**".

Many of them are ciliated "**motile**" except *Shigella and Klebsiella* are"**nonmotile**".

Many of them are intracellular pathogens.

**Slide 6:**

They might come from animal sources, or human carriers e.g *Salmonella* and *Shigella* , some small portion of people that are infected , they might be a carriers.

Enterobacteriaceae are the most common cause of gram –ve septicemias.

**Slide 7:**

So Enterobacteriaceae are gram –ve, usually motile , aerobes or facultative anaerobes and they do NOT produce spores "remember that spores are produced by gram +ve bacilli".

They are very simple in their growth requirements. The growth media shouldn't be very particular, they can grow on easy riched agar on the lab, also they are oxidase negative and catalase positive “these are important in the differentiation”

**Slide 8:**

We might use selective media (MacConkey) which is also an indicator media ( if the color changes to pink that means that the organism isolated is lactose fermenter (*E.coli)* and if not changed that means that they are lactose nonfermenor (*salmonella*)).

Classification depends on serology, DNA analysis or biochemical reactions. When we want to talk about serological mean of identification we have 3 antigens that can be used for identification: Somatic ( O antigen) part of polysaccharides “they all have lipopolysaccharide”, capsular antigen (K antigen) many of them are capsulated , flagellar antigen (H antigen) we said that many of them are motile.

**Slide 9:**

Virulence factors (pathogenicity factors) :

-Most have endotoxins because they are gram –ve bacteria.

-many have capsule (which is antiphagocytic).

-we have something called antigenic phase variations, this really has to do with antigens in flagella and other antigens, but sometimes they are expressed and sometimes are not. In the case it's expressed, we can develop antibodies against these antigens and get rid of it, but if not expressed, then antibodies will be useless. So this "antigenic phase variations factor" is important in protecting against antibodies-mediated killing.

**Slide 10:**

-exotoxins, they might have numerous exotoxins depending on the microorganism you are dealing with, some are heat labile and some are heat stable , there is also shiga and shiga-like toxins or verotoxin, which all will damage/ work on the GIT (they are Enterobactireaceae after all, so they will produce many many symptoms belonging to GIT).

We'll talk about each organism with its own toxins later.

**Slide 11:**

-expression of adhesion factors: we know that many of them have fimbriae with phase variation, which is important in adhesion to the host cell in order to establish the disease symptoms.

-intracellular survival and multiplication: many of these can live inside cells(But they don't require the cell's factors for survival, they don’t need the cell itself) and when they are inside they are protected from antibodies. So again intracellular survival is really a pathogenicity factor.

-sequestration of growth factors: we said that many of these produce siderophores that absorbs iron from surroundings (remember when we said at the beginning that iron is very important in growth of bacteria , because it’s part of many of proteins and enzymes that are produced by this bacteria).

-resistance to serum killing: many of these are resistance to cidal effect of serum (resistance to complement activation rather than antibodies which can play a role also, "the first line of defense is the complement activation of alternative pathway. " so they are resistance to it ) .

The doctor mentioned this extra information according to complement system : In general , serum killing might be heat stable(antibodie, not destoyed) or heat labile(complement system) so if we heat serum to 56ْ for about half an hour , they'll lose its complement activity.

-and also the have the ability to resist antibiotics (because they have plasmids and they can transfer it from one bacteria to another and sometimes from one species to another like from *Shigella* to *Escherichia* or vice versa ,so these plasmids will confirm antibiotics resistance on the bacteria)

**Slide 12:**

We have a lot of diseases that can be produed by these Enerobacteriaceae. Here we'll talk about them in general then later we'll talk about each bacteria.

In general these diseases can be caused by any of enterobacteriaceae but more likely to be caused by one species of organisims.

-Sepsis (septicemia) : we said that the most common cause of –ve septicemia is Enterobacteriaceae ( more likely produced by *salmonella, E.coli* and *Klebsiella*), they are pushed from GIT to blood.

-urinary tract infections(UTI) : 70% or even more of UTIs are caused by *E.coli., Klebsiella and proteus* may be also associated with UTIs. UTI more likely to be caused by microorganisms come from perineum, from flora of GIT

-Pneumonia (most likely to be associated with *Klebsiella* pneumonia).

-abdominal sepsis: if there's an abdominal sepsis this means that the bacteria comes from the contents of the intestine , so they might produce peritonitis.

-meningitis: in some cases *E.coli* might produce meningitis especially in newborns , also *Salmonella* might produce meningitis in newborns.

Meningitis might be caused by *Streptococcus Pneumonia* or *Nisseria Menegitidis* or *Listeria Monocytogenes* , but in newborns *Salmonella* and *E.coli* are mainly the cause.

-peritonitis: again it's common in pts with abdominal sepsis.

-and occasionally they might result in endocarditis.

**Slide 13:**

**-** Any infection will give you **fever.**

-occasionally, firstly u will get **Leukopenia** (drop in WBCs) then followed by **Leukocytosis** (increase in WBCs).

-Then activation of **complement** ( as we said , this will result in activation of alternative pathways)

-**Thrombocytopenia.**

**-DIC :** this is one of the complications of septicemia. Septicemia is the presence of bacteria and endotoxins in the blood, and this will result in production of a lot of cytokines as an immune response and this immune response will result in excessive adhesion of endothelial cells (endothelial cells will become sticky) so the cells will stick to them ,then there will be activation of coagulation system , and you'll get coagulation especially in small vessels , and this is known as (Disseminated intravascular coagulation, DIC).

here , platelets and coagulation factors will be used up , so as a result there will be bleeding after this DIC.

**-decreased peripheral circulation and perfusion:** because of the coagulation, and you will get major organ failure because of that

-**shock:** it's another septicemia complication.

-Finally , **Death**.

**All previously mentioned things were in general, now we will be more specific.**

**Slide 14:**

**\*** *E.coli :*

-Part of them are normal flora and some of them might be considered as pathogenic (Enerohemorrhagic *E.coli*). but the others are best described as opportunistic pathogens.

-one of the commonest diseases produces by *E.coli* is UTI (Women have short urethra in comparison to men , so women are more likely to have UTI). So this can cause urethritis, cystitis and sometimes may go up to the kidneys causing pyelonephritis.

REMEMBER: there are two types of nephritis , pylonephritis due to the presence of bacteria in parenchyma of the kidney "it's septic due to bacteria", and the other one is glomerulonephritis which is inflammation of the glomeruli due to immune mechanisms(deposition of immune complexes or by attack by antibodies)"it's nonseptic but it's due to immunological mechanisms".

-they come from perineum , and this is usually comes from intestine , the feces themselves. So in community acquired UTI , more that three quarters of the cases will be due to *E.coli.*

-Pneumoina: it’s not usual to have it,but u can have it due to *E.coli*.

-septicemia: often when we study about septicemia we will find that E.coli is one of the commonest cause.

Newborns are more susceptible to infections due to immature immune system.

Focus of infection may be from GIT or Urinary tract(UT), UTI might lead to septicemia. Also , in cases of abdominal surgeries, you mess of the intestine , you might release E.coli into the blood resulting in septicemia.

**Slide 15:**

- Neonatal meningitis : its nearly commonly produced by *E.coli*, this is obvious because some of this bacteria per canal it will be exposed to cranium and endo cranium it will be lying there ,so *E.coli* is present in the cranium.

- infections in the GIT : *E.coli* can be as part of the normal flora ,but also can cause problems in the GIT itself ,and the main symptom will be **diarrhea** ,we have variety of these strains :

1- Enterotoxigenic *E.coli* (ETEC) :

-from its name it means that they must produce the toxins that actually injures the epithelial cell of the intestine and consequently this will increase secretions and reduce absorption >> the end result is going to be a **watery diarrhea.**

-this is a common cause of **travelers diarrhea** ,some people when they travel to any place , and eat some food which is contaminated with E.coli that is new to them “ different strains of *E.coli* ” >> and these when enter the abdomen will produce toxins that will cause diarrhea.

-it's heat labile toxin ,act on the intestine ,reducing absorption and increasing secretion of water, and some can produce heat stable toxins as well.

-colonizing factor helps these bacteria to adhere to the cells and multiply

-Treatment: (in cases of watery diarrhea) you don’t have to give antibiotics, because they are almost self -limiting, and you can replace fluids if there is severe diarrhea.

**Slide 16**

2- Enteropathogenic *E.coli* (EPEC):

-they produce pathology (pathogen)

-they adhere to epithelial cell ,and do replacement of microvilli >>reduce absorption of fluids causing diarrhea “more water in the stool”.

-an important cause of **diarrhea in infants** “children are more susceptible to have diarrhea and this is because of this bacteria”

**-NOTE**: in ETEC bacteria >>diarrhea caused by the toxin.

but in EPEC >> it’s the replacement of the microvillus by the cell itself.

**slide 17**

3- Enterohemorrhagic E.coli (EHEC):

-the most pathogenic and the most serious

-it produces toxin called **verotoxin** “vero cells: are tissue culture cells they are killed by toxins produced by these bacteria”,some time they call it **shiga-like** toxin because it resembles toxins produced by *Shigella*.

-These bacteria attack the large intestine, and produce diarrhea which is **bloody**, because it injures the cells and the submucosa and leads to bleeding “that’s why its called Enterohemorrhagic”

-at the same time toxins gain access to the blood stream >> goes to the kidney and destroy it causing **acute renal failure** and that what makes this bacteria dangerous not only the bloody diarrhea

-the effect on the kidney may cause whats known as **hemolytic uremic** syndrome ,which can be very fatal.

-EHEC come with vegetables.

-The most common EHEC is O157:H7

O:somatic antigen

157: serotype

H: flagella 7 “ this is from the internet for more clarification : The antigens on the tail, or flagella are called H antigens. H7 means that this was the 7th different kind of H antigen found in E. coli”

-It can be prevented by cooking the food properly so, if you eat salad containing this bacteria (salad = uncooked) you will get the disease “always if you cook food you destroy bacteria, when you reach 70-80 degree it will die”.

**Slide 18:**

4- Enteroeinvasive *E.coli* (EIEC) :

-they invade intestinal mucosal epithelial cell.

-produce bloody diarrhea

-similar to *Shigella* “which invade the epithelial cell killing them ,cause diarrhea , produce mucous secretion and get blood in the stool”.

-in EHEC the damage done by the toxin (shiga-like toxin), while here its done by the bacteria itself (invade cells and kill them , not related to toxins ).

**slide 19:**

5-Enteroaggregative E.coli (EAEC):

-they actually aggregate ,making layers one on top of the other ,and they stick to the intestinal epithelium ,producing diarrhea.

-then they produce enterotoxin and cytotoxin which affect the epithelium “here mainly the toxin which will cause diarrhea”.

-the end result >>**diarrhea**

(sorry but you have to remember these 5 types of E.coli).

**Slide 20:**

*Salmonella*

-it has variety of types ,and their classification and nomenclature is rather complicated.

**slide 21:**

we have two types of *Salmonella*:

1-*Salmonella* which produces salmonellosis in the human being ,many many types ,some are reffered to as salmonella typhimurium , the characteristic of salmonella is that it present on the GI of animals especially birds, so if you eat something contaminated with the gut of these birds u will get salmonellosis .

-sometimes even the eggs themselves may have feces from chicken ,these may contain *Salmonella* ,so clean it and cook it well.

-also about chicken ,it may be cooked well, but sometimes when a lady cut chicken ,and then cut salad on the same cutting surface without cleaning it, you may have contaminated salad with *Salmonella*.

-so *Salmonella* can be acquired mainly from eating something contaminated with feces of bird and eggs , and very rarely to get salmonella from contamination with feces of a human carrier.

-*Salmonella* will invade the epithelial cell of the GIT,multiply there >> causing watery diarrhea “mainly” ,with some other symptoms.

-because the bacteria have to multiply ,the symptoms will not appear very quickly, they usually appear from 6-48 hr after ingestion of the *Salmonella* “there is delay” ,while toxin induced food poisoning “ by *staphylococcus*” within 1-2 hrs diarrhea appear and the symptoms disappear within 12 hrs.

-The main symptom of *Salmonella* is watery diarrhea, accompanied by vomiting ,greenish in color, and usually the diarrhea lasts for long time ,it can stay for up to a week >>which may cause a problem “dehydration” especially in the elderly and in the young people.

-*Salmonella* could be found in pigs, rodents, pets “all of which we don’t eat usually”, also turtles may be a source of *Salmonella* so if u handle them you may get salmonella

-Infecting dose usually is a big dose, so you need to have a big dose of bacteria to be able to establish themselves in the GIT.

**Slide 22:**

we will talk about the second type of salmonella which causes enteric fever later.

now ,we will continue about the one that cause salmonellosis

**slide 23:**

enteritis:

-Foodborne outbreaks

-High infectious dose

-Poultry, eggs are source of infection

-Incubation period 6-48 hr.

-Nausea and vomiting are common.

-Usually u don’t need to give antibiotics, the are not really good because they prolong the disease and they can prolong the carriage>> if you give antibiotic to *Salmonella* it will remain longer time in the gut “and produce something called the carrier stage”

- you may give fluid replacement if needed, otherwise its self limiting , you have to wait.

-In **salmonellosis you will have fever** unlike food poisoning toxin “no fever, only diarrhea and vomitting”.

-The bacteria is self multiplying and can cause infection.

**Slide 24:**

-Main symptoms is due to invasion of the GIT epithelial cells ,being destroyed by intracellular organisms, and also the production of the enterotoxins.

**Slide 25:**

-Usually S*almonella* don’t go any further, they only stay on the intestine, they may gain access to the submucosa but not any further than that (Its very unlikely to go to the blood or produce infection anywhere else).

**SO** we have 2 types of salmonella one causes diarrhea “salmonellosis” and the other causes enteric fever “typhoid fever” which is more serious and we'll talk about it later.

We mentioned each and every single word the doctor has mentioned in the lecture, but **you have to refer to the slides** , because he might have skipped some info. , saying that we took them.

Have fun .