**Shigella**

Belongs to the enter bacterium family but it's not part of the intestinal flora

- it is considered as a pathogen treated with antimicrobials because it can cause severe ulceration, blood diarrhea and may result in the death of the patient without the use of antibiotics or if the patient managed to produce specific antibodies ....

- shigella is important like salmonella because according to WHO, there are 150 million cases/year and of these, at least 1 million die especially in developing countries due to lack of treatment, diagnosis, etc.

- in contrast to salmonella, where we have two major antigens the H and somatic, here we have only the somatic antigen which means that shigella is non-motile (no H antigen which means no flagella).

- the pathogenicity is related to release of large amounts of lipopolysaccharide which is responsible for ulceration in large intestines and is associated with activation of the complement cytokines resulting in the development of thrombosis and bloody diarrhea.

- in general, all cases of shigella, whether caused by the species of any type they have the same clinical features; bloody diarrhea mainly, secondly severe abdominal pain and rarely sepsis especially in immune compromised conditions

- It's Incubation period is short, only a few cells are enough to produce infection like salmonella and associated with contamination of water and less by other means (fresh food, direct contact, etc.) exactly like salmonella.
- Water in relation to shigellosis is the main source of infection but sporadic cases may occur due to contact with person who excreted the organism or contamination of fresh food or dairy products.
- It usually multiplies in large intestine and cases more associated with large intestines and is often associated with abdominal cramps and dehydration which depends on severity of infection but can be very severe and therefore the infection requires treatment in contrast with salmonella GI which is self-limited and healthy individuals easily recover within 48 hours.
- Shigella may be complicated and may produce more side effects especially with dysenteriae which is different than others and has some special features:
  1. Blood stools, severe water bloody diarrhea
  2. Associated with special neurotoxins; *shiga toxins*. These toxins can reach the bloodstream and are carried to CNS and present the features of meningitis but it is actually because of the presence of toxins and not the bacteria.
  3. Can be so severe and may also result in more dangerous complications if it attacks the renal tissue where it will cause thrombosis and damage to kidney cells resulting in the features of *hemolytic uremic syndrome* in which patient releases blood and protein in urine and requires dialysis to metabolize the toxins or the patient will suffer from kidney failure.
- Hemolytic uremic syndrome occurs in 5% of cases of shigella dysenteriae.

**Lab Diagnosis**

4. We should take into consideration its clinical features, presence of bloody diarrhea, which are
presented by a preparation of a stool for checking the number of WBC's which are numerous like salmonella, we can culture the species on special culture like SS salmonella shigella agar and Heckton enteric HE agar to check for lactose fermenter and nonfermenter dark colonies are lactose fermenter which produces H2S that causes darkness because of the sulfur production and are associated with salmonella
- clear colonies are lactose non-fermenter shigella.
- At last some biochemical and serum test could be done to distinguish which type of shigella it is, dysenteriae or any of the others by specific antisera which are antibodies that can detect antigens

**Treatment**
- Antibiotics depend on the age of the patient, adults can be treated with ciprofloxacin doxycycline.
  14:30 the dr said another antibiotic I couldn't get it ...
- children with cotrimoxazole to reduce complications and reduce excretion of organisms in feces to reduce contamination of the environment and spread of the organism.
- infection of shigellosis is exactly like GI salmonellosis, it isn't associated with prolonged developing of protection due to the fact that shigella produces localized infection in the intestine, shigella often produces localized infection and the production of IgA but this protection is limited for 6 months to 1 year whereas salmonella (typhie and paratyphie reaches the blood stream and produces humoral antibodies) mainly IgM and IgG and is protected for many (10-20) years.
infection with shigella can occur within 1 year and is associated with specific strains because protection from one does not protect from the other types.

- more importantly, it cannot reside in the intestines for a long time which means there will be no development of healthy carriers which is important and is similar to GI salmonellosis whereas for typhi it may reside in the dispatches and gall bladder

- for that it relies mainly on preventive measures through sanitation, no need for vaccination (like salmonella) although there's a vaccine for it.

E. coli

Diarrheagenic E. coli

- E. coli is widely distributed not only in humans but animals, birds.. therefore widely distributed in nature and easily contaminates water sources, foods.

- within the group of E. coli we have 6 other types recognized as causative agents of diarrhea called diarrheagenic E. coli, these are often found at the same type with other commensal E. coli in the intestinal tract, according to the number and relation of commensal (pathogens and non-pathogens) you may not recognize their presence and not suffer from infection due to diarrheagenic E. coli.

in short, it depends on the ecological feature of your intestinal flora

- there are certain E. coli associated with production of antibody like substance colicins which can control to some extent E. coli
but any change or if you ingested a large number of diarrheagenic E. coli by food or water, you might suffer from one type or the other related to the intestine involved in watery diarrhea, watery bloody diarrhea.

1-Enterotoxigenic E. coli (ETEC) is very common and is associated with many animals and can be easily acquired by humans via contaminated water and food.

- There are two types of toxins produced by this ETEC, toxins A, B, heat labile and heat stable, both are composed of two subunits. Heat labile enterotoxigenic genes are often carried on plasma and not chromosome whereas heat stable are associated with chromosomal DNA but at the same time, E. coli that has enterotoxins of both types are found and is then associated with more severe diarrhea.

- The features are followed by adherence of the E. coli on the mucosa of the epithelial cells of the intestines (both small and large) and once attached firmly on superficial receptors of epithelial cells, these enterotoxigenic E. coli manage to damage the sub-mucosa and release lipopolysaccharides and produce toxins.

- Heat labile toxins, of two subunits, once attached and released the major B subunit and attaches to receptors, it will release subunit A which activates cAMP which indicates outpouring of water fluid, Chlorine and sodium and at the same time inhibit absorption of sodium therefore causing diarrhea whereas the heat stable toxins, the receptors are attached to subunit B and A is released but here it activates cGMP and the end result is the same, outpouring of fluid, accumulation of chloride fluid and diarrhea.

- It's often recognized development of watery diarrhea, rarely with blood but with certain
persons, it can be with blood and often without fever, vomiting may be observed but less than salmonellosis which is associated with (vomiting, diarrhea, abdominal pain, fever) with E.coli it is more like intoxication than bacterial invasion (less vomiting and diarrhea with E.coli)

- E.coli as a gram negative lactose fermenter, can be easily recognized by culture (much easier than salmonella and shigella) but it's not easy to determine whether it is enterotoxin E.coli by biochemical test - before they used mice to demonstrate presence of enlargement of intestines in fluid and recently by using special PCR we can target toxic genes by using, primary specific primers to recognize the presence of enterotoxigenic e. coli

- It's associated with famous disease known as traveler's diarrhea due to fact that in each community we are exposed as children to presence of our own strains of E. coli and therefore we've developed to some extent some level of immunity against them whereas if you travel outside the country where there are different strains especially in countries with lower standards of hygiene you will be infected because some species are associated with certain geographical regions but not it's not severe, milder, and often majority of children in the country are exposed to enterotoxigenic E. coli at least during first 10 years of life but it may be severe in certain types of patients especially in infants and neonates and…. That's why neonates should drink boiled water not even bottled water is good enough for them

2- Entero-haemorrhagic E. coli (EHEC)
- the more dangerous type and associated with larger outbreaks of diarrheal diseases and complications entero-haemorrhagic E. coli whose name indicates its association with bloody diarrhea and intestinal damage and the release of 2 types of toxins which may reach the bloodstream and get carried to the kidney causing hemolytic-uremic syndrome.

- in relation to this, they produce shiga like toxins as it was called in the past (shiga like E.coli) now it’s called vero-toxin E. coli it produces damage to vero-cells of green monkeys, still it's enough to call it entero-haemorrhagic E. coli which produce shiga like toxins.

- **shiga toxins** are of 2 types (1,2) like those of enterotoxigenic E. coli and once they reach intestinal tract they produce severe type of hematologic colitis, reach the blood stream and from blood stream to kidney and produce severe damage, thrombosis, disseminated intravascular coagulation, all in all resulting in hemolytic uremic syndrome.

- it’s often produced in outbreaks and not in single cases, in our country, we’ve had 3 studies in last 10 years and not have recognized a case of this whereas diarrhaegenic and other types have been found, that’s because these are localized mainly in the intestines of large animals especially cows any contamination in meat of cows especially grounded prepared in factories, it is associated with this organism. Recently, there was a large outbreak of hemolytic-uremic syndrome associated with this bacteria in Germany due to contamination of fresh produce, within two weeks, there were 4000 cases, bloody diarrhea, etc. and about 600 cases of hemolytic syndrome especially those above 50 years of age and of
those 600 about 50 patients died due to the complications
- this is because if they had developed signs, they must be sent to dialysis and in one or two cities, you won't find enough equipment, dialysis must also be followed up in a short period otherwise toxins will produce damage in the kidney for this hemolytic uremic syndrome is associated with high mortality rate
- treatment of both types of E. coli cannot be, to some extent, changed by antimicrobial drugs especially if toxins have reached bloodstream: therefore treatment may be helpful within the first 2 days but later, it is almost useless.
- last strains of enterohemorogenic E. coli were resistant to all classes of antibiotics except colistin and tetracyclines which were active and other drugs cannot be used due to presence of extended spectrum beta-lactamase enzymes in these strains
- they acquire the toxin in association with antimicrobial resistant factors through transmission of conjugative plasmid
- this type has caused outbreaks in Japan, USA, Canada due to hamburger consumption... Japan more than 1,000 were suffering from hemorrhagic diarrhea

3-Entero-pathogenic E.coli (EPEC)
- It is of less importance, often associated of infection of young infants up to 6 months of age.
- It's usually associated with mild diarrhea but could be severely dangerous because it is not easily recognized by the mother and the child may develop chronicity which may result in death
- later infants develop specific localized immunity preventing the occurrence of disease and also relieving the patient.
- older children and adults are immune normally.
- it's virulence is related only to polysaccharide capsules found on the cell wall of organism.
- it's dangerous only if chronic diarrhea continues then treatment with antimicrobial drugs is a must to stop chronic diarrhea, often this chronic diarrhea is not easily controlled in infected infants.

**4-Entero-invasive E.coli (EIEC)**

- similar to shigella
- associated with localized inflammatory reaction in intestines in form of enterocolitis or ulcerations associated with watery bloody diarrhea and less vomiting but abdominal pain and fever exactly like shigella.
- rarely reaches bloodstream but it may do especially in infants (sepsis).
- happens often in children or first-contact adults especially those who developed travelers diarrhea traveling to developing countries exactly like enteroxigenic E.coli which produces traveler's diarrhea.

**Lab diagnosis**

- based on culture, isolation especially on MacConkey, look for a type of organism by PCR (molecular techniques).
- using specific anti-serum and biochemical tests cannot identify exactly this group of E.coli, the only way to look for specific primer in the DNA of these E. coli and recognize specific type.
treatment
- entero-haemorrhagic and invasive are treated in the first phase in relation to diarrhea, you determine it's there by special culture media similar to MacConkey with lysine sugars incorporated to recognize presence these types
- the way to simple recognition is by numerous WBC's and SS agar to exclude shigella and salmonella and then molecular technique.
- up to date no vaccine available despite the fact they've prepared toxins for animals against enterotoxigenic E. coli especially in animals, chickens since it's associated with sepsis and loss of life for these animals: vaccine for animals and not humans and these toxins might produce side effects.

in the first of few minutes of the lecture the Dr said something about salmonella, here it is

- typhoid fever is associated with infection caused by salmonella typhi and paratyphi A, B, V.
- in clinical cases, impossible to distinguish between typhi and paratyphi and the only way is to isolate them in culture, blood culture, urine, CSF, blood culture or feces.
- typhi and paratyphi bacterial species are associated with the same clinical features, all the details related to one is related to the other
- the second type is related to GI salmonellosis caused by other species and strains and produces
localized infection of intestines associated with diarrhea and rarely reaches bloodstream to cause systemic infection like typhoid fever especially in neonates and patients with immunodeficiency

in relation to diagnosis, isolation of organism is important whereas serological detection of specific antibodies is more important in association with typhoidal fever and not GI because although it produces immunoglobulins especially IgM, IgG it is in small amounts that it can't be used for the detection of salmonella GI. And for this Widal test is related to typhe and paratyph (mainly typhe) and not GI. In practice the importance of recognizing the serotype is for epidemiological studies (the source of the infection and how to follow it in the community) not for treatment.

Done By:

Marina Zawaideh