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Campylobacter :

These organisms were formerly grouped with Vibrios and were known as animal pathogens *Campylobacter jejuni* and *Campylobacter coli* have emerged as common human pathogens , they are commonly causing diarrhea .

Morphology and cultural characters:

They are gram negative rods with comma or S or gull-wing shape ,they are motile with single polar flagellum and do not form spores . microaerophilic (incubation must be in an atmosphere with reduced Oxygen tension , 5-10% CO2 is required through incubation in Gas pack Jar supplied with Gas generating kit . Incubation of primary plates should beat 42-43 C to prohibit growth of most of other bacteria present in feces. Several selective media are widely used such as Skirrows medium incorporates Vancomycin , Polymyxin B and Trimethoprim .

Colonies tend to be colorless or grey , they may be watery and spreading on the surface of the medium or round and convex .

***C. jejuni* and other species pathogenic for humans are Oxidase and catalase positive do not oxidize or ferment carbohydrate.**

Pathogenesis: The infection is acquired by feco- oral route through food and drinks , contact with infected animal . Mean infective dose is 10^4 organisms , this inoculum is similar to that required for Salmonella and Shigella infection. The organism multiply in the small intestine , invade intestinal mucosa and produce an endotoxin similar to that of *Vibrio cholera*. The organism multiply in small intestine , invade the epithelial cells and cause inflammation that results in the appearance of white and red blood cells in the stool that results in the appearance of foul smelling bloody diarrhea . occasionally the blood stream is invaded and a clinical picture of enteric fever develops.

Clinical findings :

Acute onset of cramps ,abdominal pain and diarrhea that may be grossly bloody , headache , malaise and fever . It is self limiting illness occurs within 5-8 days .

Laboratory diagnosis :

1- Stool specimen is suitable for the lab diagnosis in bloody diarrhea through :

- **a- direct identification by Gram stain to reveal S or Gull wing shape like gram negative organisms .**
- **b- Dark field microscopy to show Darting motility of the organisms.**
- **c- Cultivation on Selective medium Skirrows medium under suitable conditions show gray color mucoid circular opaque colonies.**

2-blood specimen is indicated in case of septicemia.

Helicobacter pylori :

It was formerly known as *Campylobacter pylori* . It is an important human pathogen has been emerged in the last few years after 1990. It is either S or spiral shape actively motile by multiple polar flagella. Clinically this organism was found responsible for the most common chronic bacterial infection. It is responsible for an estimate 90% of gastric ulcer pyloric ulcer which one thought to be result from stress induced stomach acids. Some individuals can harbor these pathogens for years with no illness , while other develop ulcer or gastric disease including active chronic gastritis , PU , DU and gastric cancer which is a common malignancy in Eastern Europe , Latin America and Asia.

***H. pylori* uses several mechanisms to escape the most immune response to adapt to the changes in gastric environment.**

Mode of transmission is the feco-oral route through contaminated food and drinks.

General activities of *H. pylori*

It has ability to colonize the mucosa of the stomach

Rapid urease activity which is useful in its identification

It resists high acidity of stomach, it has ability to degenerate mucin and many degenerative adhesions were identified with the products of enterotoxin and protease. This is associated with the production of DU . It was found that different strains of *H. pylori* ,this explain why some people are affected while others are not.

Lab diagnosis:

1-biopsy is the suitable specimen for the isolation of *H. pylori* and urease test

Cultivation and Identification of organism on Skirrows medium

Serology to identify IgM and IgG , her IgG against *H. pylori* has no role in killing organism , but it may be helpful in the epidemiology studies.

Urea breath test:

This test depends on the rapid urease activity of *H. pylori* .

When Patient is given C^{14} labeled urea with water , urease enzyme of the organism splits urea into ammonia and CO2. Released CO2 can be detected in the expiration of patient and measurement of labeled carbon .

Yersinia , Francisella and Psteurella

These organisms are short pleomorphic gram negative rods that can exhibit bipolar staining, non spore forming an aerobic.

Animals are their natural hosts, but they can produce serious human diseases.

Yersinia:

There are three important species within this genus :

Yersinia pestis* , *Yersinia pseudotuberculosis* ,and *Yersinia enterocolitica

Yersinia pestis:

It is Gram negative short plumb rods that exhibits bipolar staining with special stain like safety pin .

It is facultative an aerobic, optimal temperature for growth is 30C. Growth is more rapid in media containing blood or tissue fluids. Virulent inoculum produce gray viscous colonies which rough after passage.

Antigenic structure:

Yersinia pestis **has lipopolysaccharide antigen that have endotoxin activity when it is released. The organism produce many antigens and toxins that act as virulence factors:**

1- **The bacteria have type-3 secretion system that consists of a membrane- spanning complex that allows bacteria to inject proteins directly in the cytoplasm of the host cells.**

2- **The virulent strains of *Yersiniae* produce *V* and *W* antigens, which are encoded on a plasmid. These antigens yield the requirement for calcium for growth at 37C.**

3- **Capsular protein fraction -1 is mainly produced at 37C and antiphagocytic activity**

4- **It has Pathogenicity island PAI that encodes for Iron scavenging siderophores.**

Pathogenesis:

Yersinia pestis **causes plague which is an infection of wild rodents transmitted to humans by flea bites. When flea feeds on**

rodent infected with *Yersinia pestis* , the ingested organism multiply in the gut of the flea and transmitted by subsequent bite. The inoculated organism may be phagocytized, organisms multiply (intra or extra cellular), they reach lymphatics leading to hemorrhagic lymphadenitis. Organisms often reach blood stream and disseminated hemorrhagic necrotic lesions may develop in all organs. Meningitis, pneumonia and pleuropericarditis are prominent.

Primary pulmonary plague may results from inhalation of droplets, which leads to hemorrhagic lobar pneumonia.

These pathologic processes are due to antiphagocytic effect of antigens and intracellular toxins that act on vascular system causing irreversible shock and death.

Clinical findings:

The incubation period is short, 2-7 days. There are three clinical forms of pestis:

1- Lymphadenopathy (bubonic plague):

Enlargement of axillary, groin lymph nodes, it is highly fatal characterized by chills, fever nausea, vomiting and diarrhea.

This type is transmitted to human by bite of infected rat fleas.

2- Primary septicemia form:

It resembles bubonic type except that bubones are not formed.

3- Primary pulmonary type :

It is sudden and severe resulting in respiratory distress and death.

It involves lungs and leads to lobar pneumonia and it is contagious by droplet infection.

Laboratory diagnosis:

Specimens from patients are blood, sputum, CSF and lymph aspirate from lymph nodes.

1- Direct examination of the specimen using smear staining with bipolar stain.

Observations: Examined smear under oil immersion lens of light microscope reveals Gram negative pleomorphic rods look like safety Pin appearance.

2-Immune Fluorescent technique reveals fluorescent organisms under UV light microscope.

3-Cultivation on blood agar and MacConkey agar and infusion broth.

Growth on solid media may be slow, but blood cultures are often positive in24 hours. Cultures can be identified by biochemical reactions. Definite identification of culture is best done by immunofluorescence. All cultures are highly infectious and must be handled with extreme caution.

4-Serology:

In patient who have not been previously vaccinated, a convalescent serum antibody titer of (1: 16) is considered presumptive evidence of Y. pestis infection. A titer rise in two sequential serum antibody titer confirms the serologic diagnosis.

Treatment:

Unless treated, plague may cause 50% mortality. Pneumonic plague show 100% mortality. The drug of choice is Streptomycin, tetracycline is also effective.

Control :

Formalin killed vaccine is available for the travelers to endemic areas, solid immunity to plague develops following infection.

Yersinia enterocolitica, Yersinia pseudotuberculosis

They found normally in the intestine of some animals. It cause febrile diarrhea in human and abdominal pain due to endotoxin production which is similar to that of *E coli.* It is non lactose fermenting Gram negative rods that are urease positive and oxidase negative. They grow best at 25 C and motile at 25C but non motile at 37 C.

Lab diagnosis:

1-Direct staining technique.

2-Culture : The number of Yersiniae may be small in stool and can be increased by cold enrichment, small amount of feces or rectal ph 7.6 and kept at 4C for 2-4 weeks . Many fecal organisms do not survive but Y. *enterocolitica* will multiply subcultures made at intervals on MacConkey agar may yields *Yersinia* .

3-Serology: Cross reactions between Yersiniae and other organisms (Vibrios, Salmonella, Brucella) may confuse these results.

Treatment :

Gentamicin , Streptomycin are effective.

Pasteurella

They are primarily animal pathogens but they can produce range of human diseases. Pasteurellae are Gram negative coccobacilli non motile showing bipolar appearance with bipolar stain. They are aerobic and facultative anaerobic. They grow on ordinary media at 37c and they are oxidase and catalase positive but diverge in other biochemical reactions.

P. Multocida

It occur world-wide in the upper respiratory tract and digestive tract of domestic and wild animals. It is the commonest organism in humans infected wound due to animal bites like cats dogs etc.

It cause hemorrhagic septicemia in domestic animals.

Clinical presentation:

The most common presentation is an animal bite with acute onset of redness, swelling and pain are within bites regional lymph nodes are enlarged with low grade fever. Sometime Pasteurella infections present as bacteremia or chronic respiratory infections without any evidence of animal contact.

Francisella tularensis

It is widely found in anima reservoir primarily wild rats and it is transmissible to humans by biting arthropods (fleas or ticks), direct contact with the infected animal, inhalation or ingestion of contaminated food or water. The resulting disease is Tularemia.

Morphology:

***Francisella tularensis* is a small gram negative coccobacillus or pleomorphic rods non motile. Growth is difficult on ordinary media. growth requires media enriched with Cystien , in the past glucose –Cystien blood agar was preferred but Francisella tularensis grows on hemin containing media like chocolate agar , modified Thayer martin agar , and buffered charcoal yeast extract (BCYE) used to grow Legionella species .**

Cultivated media should be kept at 35-37 C for 3-5 days under aerobic conditions. Caution must be taken using biosafety level 3.

Pathogenesis:

***Francisella tularensis* is highly infectious contagious enter human body by three methods, respiratory, skin or mucous membranes and ingestion, the infective dose is 50 bacterial cells.**

Most commonly organisms enter through skin abrasions in 2-6 days. An inflammatory ulcerating papule develops. Regional lymph nodes enlarge and may become necrotic, sometimes draining for weeks ulceroglandular tularemia.

Inhalation of infective aerosol results in peribronchial inflammation and localized pneumonitis (pulmonary tularemia).

Oculoglandular tularemia can develop when an infected finger or droplet touches the conjunctiva . yellowish Granulomatous lesions on the lids may be accompanied by preauricular adenopathy .

The other forms of disease are oropharyngeal tularemia , typhoidal (septicemia) and glandular tularemia (Lymphadenopathy but no ulceration). In all cases there is fever , malaise , headache and pain in the involved region and regional lymph nodes . because of highly infectious nature of f t , this organism is a potential agent of bioterrorism.

Lab diagnosis :

Though *Francisella tularensis* may be recovered from clinical specimens , diagnosis rests on the serologic studies. Paired serum samples collected two week a part can show a rise in agglutination titer.

A single serum titer of 1 160 is highly suggestive if the clinical findings are compatible with the diagnosis .

Because antibodies reactive in the agglutination test for tularemia also react in the test for brucellosis , the titer for the disease is affecting the patient is usually fourfold greater than that for other disease.

Treatment :

Streptomycin or gentamicin therapy for 10 days produces improvement.