Pathogens causing Diarrhea and Dysentry I
Bacterial and Viral pathogens

Learning Objectives

At the end of the session the student should be able to:
- Define diarrhea and dysentery and list the underlying causative pathogens
- Describe pathogenesis of common gastrointestinal infections including diarrhea and food poisoning
- List the relevant diagnostic tests

BACTERIA CAUSING DIARRHEA & FOOD POISONING

- Staphylococci cause food poisoning
- Bacillus cereus
- Clostridium difficile
- Clostridium perfringens
- Clostridium botulinum
- E.coli
- Salmonella
- Shigella
- Vibrio cholerae
- Campylobacter and Helicobacter

PATHOGENESIS OF STAPHYLOCOCCAL FOOD POISONING

- Bacteria get deposited in food
- Caused by enterotoxin which is resistant to heat, gastric acid & jejunal enzymes.
- It acts as a super-antigen causing release of IL-1, and IL-2. Cytokines act on vomiting centre in the brain.

BACILLUS CEREUS

- A gram positive, aerobic and spore forming bacterium.
- Spores on cereal grains such as rice survive steaming & rapid frying and germinate when the food is kept warm for many hours (reheating).
- Enters via GIT
Pathogenesis

*Produce 2 enterotoxins:*
- Causes ribosylation of ADP of a G protein which stimulates adenylate cyclase resulting in increased concentration of cyclic AMP within the enterocyte.
- The other enterotoxin acts as a super antigen

*Two types of syndromes occur:*
- A short incubation period (4hrs) after which nausea, vomiting occurs.
- A longer incubation period (18 hrs) characterized by watery non bloody diarrhea.

**CLOSTRIDIAL FOOD POISONING**
- Transmitted by contaminated food.
- Protein rich foods e.g. meat & beans favor the growth of soil borne spores into vegetative cells that produce potent Exotoxin & is consumed in food.
- Resulting in malabsorption & diarrhea.
- Organisms can be isolated in a large # from the remains of food

**CLOSTRIDIUM DIFFICILE**
- A gram +ve bacillus.
- Causes antibiotic associated pseudo-membranous colitis.
- Approximately 3% of general population and 30% of hospitalized pts. carry this organism.
- Can be transmitted by faecal – oral route

**Pathogenesis**
- Long term administration of antibiotics causes suppression of sensitive microorganisms, allowing C.difficile to multiply & produce exotoxins of 2 types.
- The exotoxins causes cytoskeletal destruction, apoptosis & death of enterocytes.

**Signs & Symptoms**
- Pts on prolonged therapy by Clindamycin, 2nd & 3rd generation cephalosporins and cancer chemotherapy, suffer from non bloody diarrhea, fever & abdominal cramps.
• Toxic megacolon may occur.

• Yellow white plaques can be visualized on colonic mucosa.

**Lab. Diagnosis & treatment**

• The stool sample filtrate shows presence of exotoxins by ELISA.
• Cytotoxicity test.

• Treatment: Withdrawal of causative antibiotic

**CLOSTRIDIUM BOTULINUM**

• A gram +ve anaerobic spore forming bacillus.
• Transmitted through contaminated food mostly improperly sterilized home-canned food, alkaline vegetables, e.g. green beans, peppers, mushrooms & smoked fish.
• Spores are wide spread in soil.

**Pathogenesis**

• Toxin is produced within the canned food.
• When consumed the toxin is absorbed in the gut & reaches the peripheral nerve synapses via the blood.
• The toxin blocks release of acetylcholine.
• Botulinum toxin can be demonstrated in samples from food & pts. serum.

**BACTERIAL CAUSES**

**Enterobacteriaceae**

• Gram negative facultative anaerobic rods oxidase negative (no cytochrome oxidase)
• Serotypes: antigenic types
  • O (lipopolysaccharide)
  • H (flagellar)
  • K (capsular)
E. coli

Lactose Positive

**Enterotoxigenic E. coli**
- Causes Travellers diarrhea
- Heat labile toxin like choleraogen
  - Adenyl cyclase activated
  - cyclic AMP
  - secretion water/ions
- Heat stable toxin
  - Guanylate cyclase activated
  - cyclic GMP
  - uptake water/ions

**Enteropathogenic E. coli**
- Causes destruction of surface microvilli
- Fever, non-bloody diarrhea, nausea and vomiting

**Enteroinvasive E. coli (EIEC)**
- Causes Dysentery, resembling shigellosis

**Enterohemorrhagic E. coli**

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**SHIGELLA**
- *S. flexneri, S. boydii, S. sonnei, S. dysenteriae*
  - Causes bacillary dysentery
  - Man is the only reservoir
  - Fecal to oral contact
- Mostly young children in nurseries and daycare
  - transmitted by adult food handler

**Shigellosis**
- Bloody feces
- Intestinal pain
- Pus
- shiga toxin

**SALMONELLA**

*S. enteritidis*
- The common salmonella infection
- Poultry, eggs
- No human reservoir
- Gastroenteritis
  - Nausea
  - Vomiting
  - Non-bloody stool
  - Self-limiting (2 - 5 days)

**Salmonella typhi**
- Enteric fever
- May cause epidemics
- Severest salmonella disease. Rare in US human reservoir
  - Carrier state common
- Contaminated food
- Water supply
- Poor sanitary conditions

**YERSINIA ENTERCOLITICA**
- Gastroenteritis
- Common in Scandinavia, also in US (colder regions)
- Transmission through fecal contamination, domestic animals
  - Water
  - Milk
  - Meat

**VIBRIO CHOLERAE**
- Gram negative comma shaped rods
- Facultative oxidase positive anaerobes
- Simple nutritional requirements
- Readily cultivated
- Cause epidemics in the third world but uncommon in the US
- Causes infections in travelers
- Ingestion of sea-food

**A-B toxins**

Cholera toxin - Choleragen
• B binds to gangliosides
• provides channel for A
• A catalyses ADP-ribosylation
  — regulator complex
  — activates adenylate cyclase

**Exotoxins**
Results in loss of water and ions from the cell.
• The genes for the toxin are carried on a single stranded DNA bacteriophage called CTX.
• The watery efflux enters the lumen of the gut resulting in massive diarrhoea without neutrophils or RBC.

**Clinical findings**
• Watery diarrhoea in large volumes.
• Typical rice–water stools
• There is no abdominal pain.
• Severe loss of fluids and electrolytes may lead to cardiac and renal failure.
• Acidosis and hypokalemia (loss of bicarbonate and potassium).

**Lab. Diagnosis**
• Culture of diarrhoeal stool on MacConkey’s agar shows colourless colonies (slow lactose fermenter).
• Oxidase positive.
• Acid slant and acidic butt on TSI.
• Agglutination with polyvalent O1 antisera or non O1 antisera.

**CAMPYLOBACTER**
• Gram negative rods
• Curved or spiral
• Genetically related
• Infects the intestinal tract of animals
• Cattle and sheep
• Major cause of abortions in cattle
• Micro-aerophilic and grows best 42°c
• Diarrhea
• Malaise
• Fever
• Abdominal pain

**HELICOBACTER**
• These are gram negative curved rods similar to campylobacter but differ significantly in certain biochemical and flagellar characteristics.
• Strongly urease positive (campylobacters are urease negative).
• Attack stomach mucosa and cause gastritis and peptic ulcers.
• Linked to gastric carcinoma and mucosal associated lymphoid tissue (MALT) lymphoma

**H. PYLORI**

• H pylori attaches to the mucus secreting cells of the gastric mucosa.

• A large amount of ammonia is produced from urea due to the urease produced by the microorganisms coupled with inflammatory response that leads to damage to the gastric mucosa and loss of protective mucus coating predisposing to gastric and peptic ulcers.

• The ammonia also neutralizes gastric acid and allows the organisms to survive.

**Lab. Tests diagnosis**

• culture
• Endoscopy and gastric mucosal
• Urea breath test
• radioactive CO2 breath after feeding radioactive urea
• Immunodiagnosis of helicobacter pylori IgG antibodies in the patients serum and detection of antigens can be done.

**VIRAL PATHOGENS CAUSING DIARRHEA**

• Rotavirus
• Enteric adenoviruses
• Calicivirus
• Astrovirus

**ROTAVIRUS**

• First isolated in 1973 from children with diarrhea.
• A major cause of diarrhea-associated hospitalizations esp. in children
• Incubation period- thought to be <4 days. Mainly person to person via fecal-oral route, fomites
• Food and water-borne spread is possible
• EM appearance of a wheel with radiating spokes
  • Non-enveloped Double capsid icosahedral virus with double stranded (ds) RNA in 11 segments

**Pathogenesis**

• resistant to handwashing agents
• Susceptible to disinfection with 95% ethanol, ‘Lysol’, formalin Attacks mature enterocytes lining the tips of intestinal villi by entering through endocytosis
• Virus replicates in the host cell cytoplasm
• Infiltration of lamina propria with mononuclear cells
• Repopulation of the villous tips with immature secretory cells [crypt hyperplasia]
• Results in villous atrophy, blunting and cell death

Histopathology

ENTERIC ADENOVIRUS
• Incubation period 3-10 days
• Diarrhea lasts for 10-14 days
• Can also cause intussusceptions, mesenteric adenitis, appendicitis

NORWALK VIRUS
• A Calicivirus
• Most common cause of epidemic viral gastroenteritis in adults
• Fecal oral spread
• Incubation period is 24-48 hrs
• Lab. diagnosis by ELISA

REFERENCES
• MICROBIOLOGY By JAWETZ
25TH EDITION