

# Digestive System

University of Jordan  
Faculty of Medicine  
Batch of 2013-2019



Slide  Sheet  Handout  Other

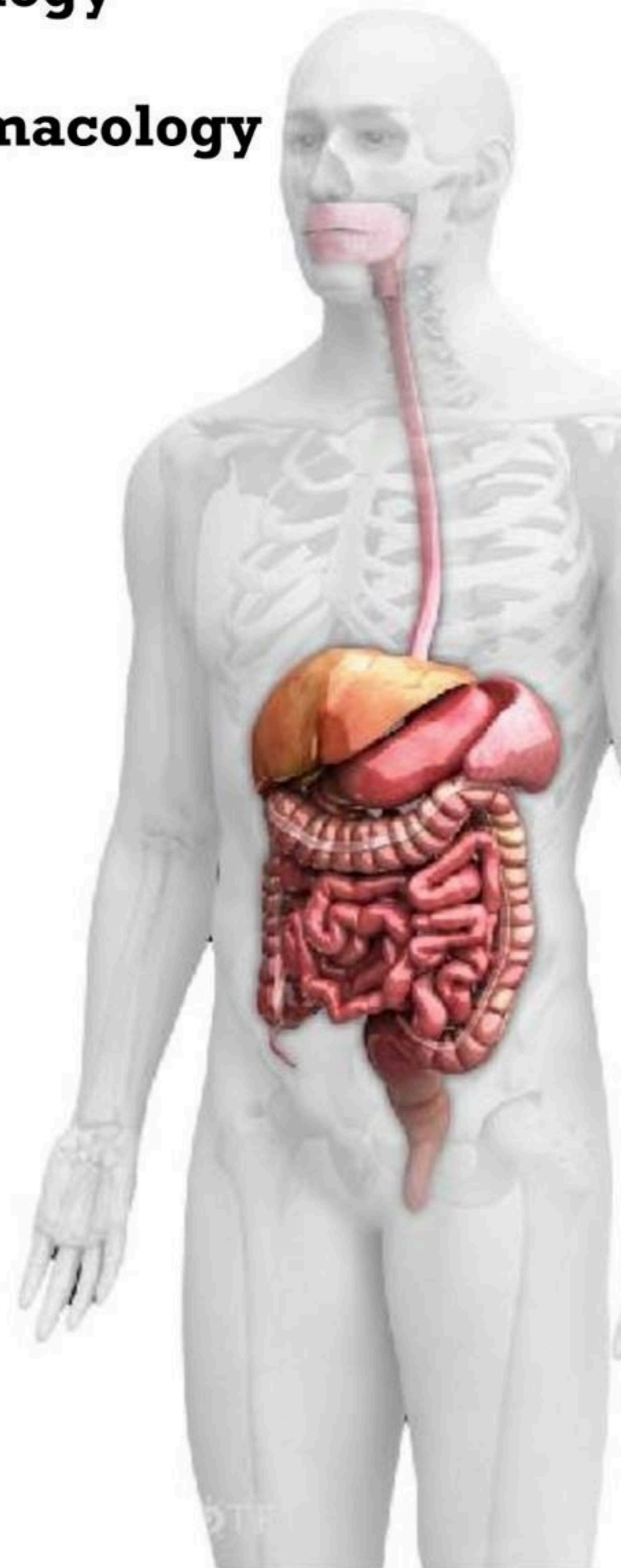
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**Slide #:** Bacteriology Slides

**Doctor:** Asem Shehabi

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**Price:**



# **Bacterial Gastrointestinal Infection**

## **2-Year Medical Students**

Prof .Dr. Asem Shehabi

Faculty of Medicine

University of Jordan

# Introduction

- Worldwide, At least one **billion of children & adults** are affected by diarrhea each year. In developing countries, where general sanitation is low, epidemics of bacterial gastroenteritis cause high morbidity & mortality among infants & children .
- The commonest clinical manifestations of bacterial gastrointestinal infections are : **Diarrhea, vomiting , abdominal pain, fever.**
- Bacterial intestinal infection..followed water/Food contamination.. incubation period 8-24 hrs .. rarely involve other organs and systems.. Recovery 2 days
- Watery diarrhea..involved small and large intestines
- Bloody-diarrhea (Dysentery ) mostly Large intestine
- **Enterocolitis** inflammation of both small & large intestines,..bacteria & toxin..watery bloody diarrhea

# Bacteria Food poisoning

- **Bacterial food poisoning** ..Foodborne intoxication is another common cause GI illness associated with the presence of a pre-formed toxin in food released by **Toxigenic bacteria**.. Mostly first associated with vomiting & later watery diarrhea.. No fever.. Short incubation period..2-8 hours
- In many cases the toxin may be produced in the food by bacterial growth during storage or preparation.. Due to hand or environmental contamination.
- **Common Gram-ve:** *Salmonella spp.*, Various types diarrheagenic *E. coli* strains, *Campylobacter spp.*, *V. cholerae*, *Listeria* & *Aeromonas spp.*
- **Gram-positive :** *Staphylococcus aureus*, *Bacillus cereus*, *Cl. perfringens*

# Salmonella Group

- **Salmonellae group:** Gram-negative bacilli, Facultative anaerobes.. By current classification there is only one major species of Salmonella: *S. enterica*.. but there are numerous serotypes .. about 2000 types
- A serotype is classified by presence of a specific set of O (cell wall) ,H (flagellar), Vi (virulence) antigens.
- **Human Salmonellosis** is divided into:
  - 1- **Enteric Fever Salmonellas /Typhoid fever**.. infect only humans caused by *enterica subtype Typhi & Paratyphi A, B, C*.. Cause severe human systemic diseases.. following invading GI with few salmonella cells..often through contaminated water..Less fresh Food, rarely direct contact.. Incubation period **1-3 weeks**.

# Typhoid fever-2

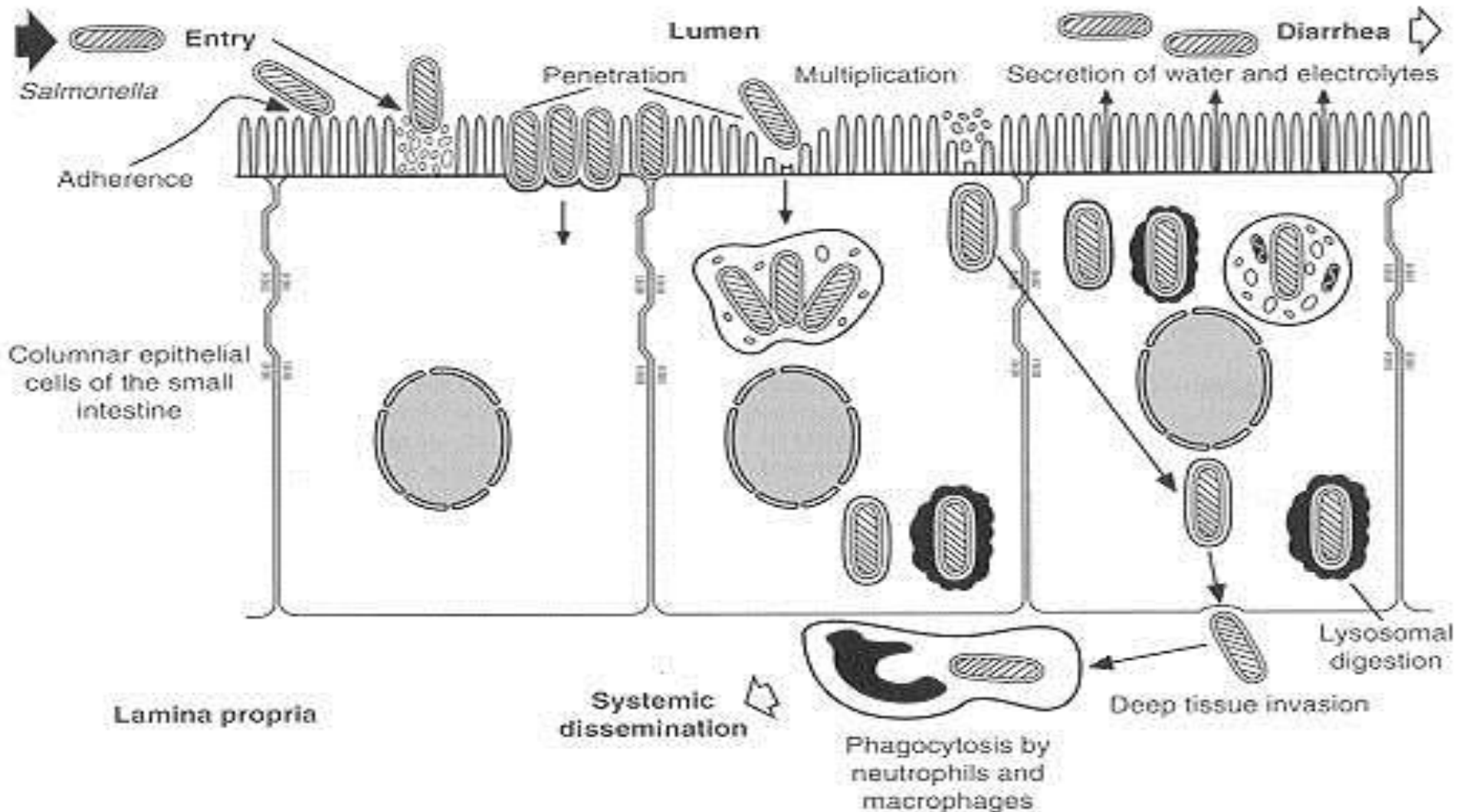
- Typhoid fever is a severe **multisystemic illness**.. Salmonella invade & multiply within intestinal mucosa .. Peyer patches. Enter intestinal lymphoid follicles.. Macrophages carry cells to Reticuloendothelial system ..Causing Lymphoid hyperplasia & hypertrophy later spread to Blood, liver and other internal organs..
- **Typhoid Fever** is characterized by the prolonged & high fever, headache, malaise, liver & spleen enlargement ..Skin rash (Rose spots)..Mostly watery- bloody diarrhea /constipation at the beginning. **Pathogenicity**: Virulence factors.. Proteinous capsule (S. typhi Vi antigen), Cell wall Lipopolysaccharides, release specific cytotoxins.

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# Salmonella-Typhoid Fever -2

- Following blood sepsis ..necrosis of liver & spleen, gallbladder. lymph tissues, peyer patches.. Salmonella re-enter intestinal tract.. causing severe intestinal inflammation, bloody diarrhea, enterocolitis, intestinal perforation & toxic shock. **10-30%** of patients might die without antibiotic treatment.
- **Typhoid fever** may be associated with meningitis, mostly in children & immune deficiency.
- **Complications** presented as pneumonia, endocarditis, osteomyelitis, septic arthritis, hepatic abscesses, soft tissue abscesses in any body part.

# Process of Typhoidal Salmonella Infection





# Typhoid fever-3

- Up to 5% of infected persons become later **healthy carriers**..Females more than Males..Infection becomes chronic.. Carry the bacteria in their **Gallbladder**.. Less in **Peyer patches**.. excrete bacteria in their feces for long live.
- **Healthy carriers** maintain the cycle of Typhoid disease in the community.
- Host responded to infection by production of specific antibodies (**Anti-O & anti-H**) which can be detected after 2 weeks.
- **Typhoidal antibodies** might prevent developing of severe complications and death.

# Lab Diagnosis

- **Definitive diagnosis Typhoid Fever:** Requires culture & isolation of the organism from blood, Feces, CSF, Urine according acute/sub-acute/chronic cases.
- **Chronic cases..** bone marrow, Gallbladder.. Healthy Carriers.. excrete occasionally bacteria in stool.
- Presence *S. typhi* only in stool without clinical disease indicates carriage state.
- **Selective culture media:** S-S agar, Heckton-enteric agar... Lactose non-fermenter bacteria growth
- **Serological test:** Widal test is used for the diagnosis of Typhoid fever.. measures levels of antibodies against (O, H ) antigens.. Titer > 160 or **rising titers..** positive (Vi ) antigen indicate *S. typhi*.. acute infection.

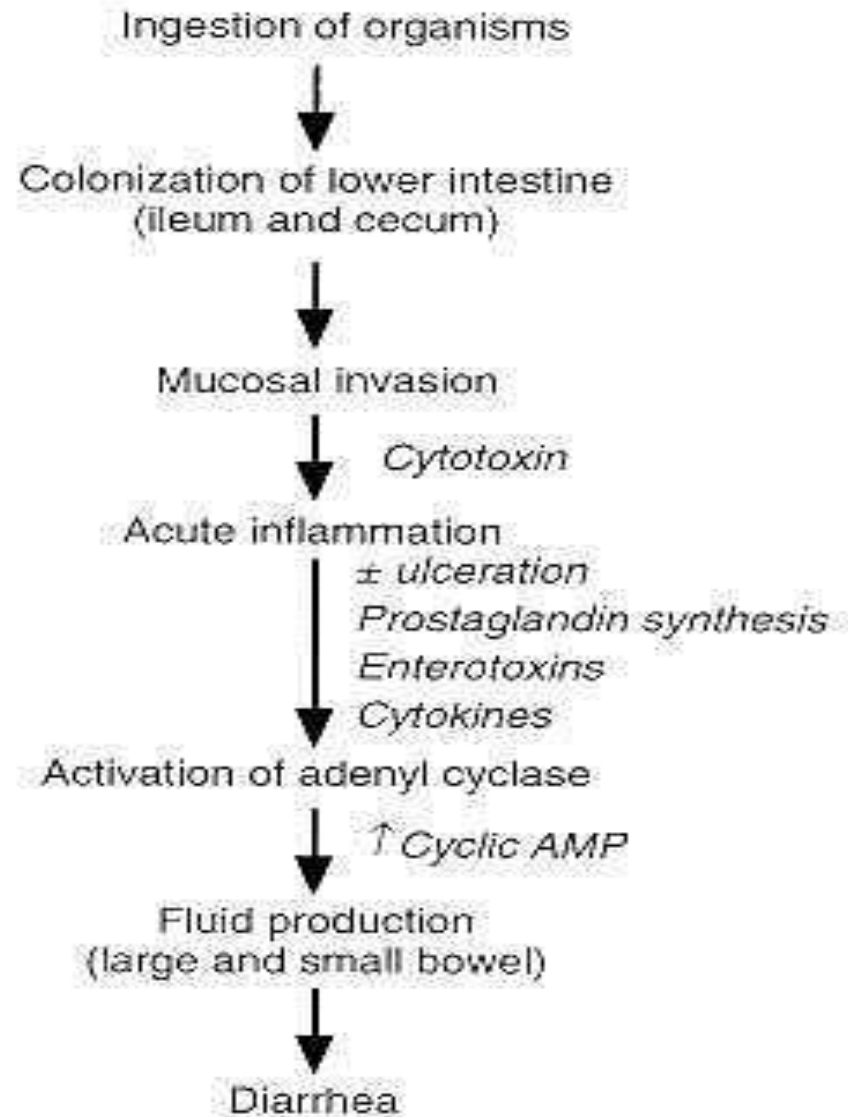
# Treatment & Prevention

- **Antibiotic therapy** is essential and should begin empirically if clinical evidence of infection is strong.. Ciprofloxacin 4 weeks.. Ceftriaxone for pregnant women & Children.. Chloramphenicol & Amoxicillin/ Augmentin is currently less used due to resistance.
- **Fatality** is high without antibiotic treatment
- **Typhoidal Salmonella**.. Endemic in most developing countries.
- **Public health measures**: Control safe drinking water, proper sewage disposal, Detection human carries, Food hygiene.
- Oral live attenuated Tyhoid vaccine / injectable **vi-capsular polysaccharide vaccine** can be used for short protection in endemic region.

# Gastroenteritis/ Food-Poisoning Salmonellas-2

- **S. enterica var Typhimurium and S. enterica var Enteritidis** .. are most common serotypes of GI Salmonellosis in humans, Birds/chicken, animals, Rats. Each year Million food-borne cases worldwide, single & outbreaks..Contaminate commonly human fresh prepared food..**Grounded meat & Eggs.**
- After Salmonella ingestion.. **Incubation 8-24 hrs**, watery-bloody diarrhea, Less vomiting, abdominal pain, fever..1-2 days.
- **Complications:** septicemia, meningitis observed mostly in neonates, infant, immunosuppressed patients.
- **Pathogenesis: Salmonella** following invade epithelial cells small intestine, release cytotoxin causes inflammatory response.. activation mucosal **Adenylate cyclase** which stimulates **cAMP**.. results in intense & prolonged hypersecretion chlorides ions & water, inhibiting reabsorption of sodium.

# Intestinal Salmonella Infections



# Gastroenteritis Salmonellas-2

- **No antimicrobial drugs treatment..** For normal healthy persons.. Only Rehydration.. Antimicrobial drugs should be given for infants & immuno-suppressed patients.
- Rare & Short human healthy carriers in intestine.. Clinical cases excrete salmonella for few days-weeks in feces- short-period healthy carrier.
- **Stool culture** in S-S agar, Heckton-enteric agar
- Prevention hand-food contamination.. often Chicken eggs & meat & Dairy products, mayonnaise
- **Widal test is not significant in diagnosis of infection.** No human vaccine is available.. chicken vaccine

# Shigellosis-1

- ***Shigella spp*** continue to be a major health problem worldwide, causing an estimated 1 million deaths and about 150 million cases of diarrhea annually. **Shigella** are Gram-negative, Lactose-ve bacilli.. Facultative Anaerobes.. Highly susceptible to dryness.. Acidity.. killed within 1 hour in stool.
- **Main 4 species of Shigella:** *S. dysenteriae*, *S. sonnei* , *S.boydii*, *S. flexneri*..Infect only humans.
- **Shigellae** cells invade, multiply in mucosa of large intestine, cause swelling & necrosis intestinal wall due to cytotoxin & endotoxin.. Watery-bloody diarrhea, severe abdominal cramps, high fever & nausea.. less vomiting, **feces** contains numerous WBCs & mucus, **Incub period within 24 hrs**..Rarely blood sepsis

# Shigellosis-2

- **Clinical disease** ranges from mild diarrhea to dysentery..few days, Most deaths occur in young children / elderly persons due to dehydration & blood loss. Only Human infection. **highly infectious & communicable** ..Person to person contact, water, fresh green leaf vegetables.
- **Dysenteriae** is the classic cause of bacillary dysentery ..**Sh. Dysenteriae**: severe necrosis, muco-purulent bloody diarrhea, severe abdominal pain, high fever..more bloody diarrhea & dehydration
- Release heat-labile **Shiga enterotoxin** (neurotoxin).. affects small intestine.. carried to blood, CNS.. causes mild-severe meningism & comma.. Few cases hemolytic-uremic syndrome. Death rate is high in patients not treated..Septicemia is rare .



# Diagnosis & treatment

- Acute Shigella case: Direct stool examination for presence of numerous **WBCs and blood cells**
- Direct rectal swab.. or rapid stool culture of feces on S-S agar, Heckton-enteric agar.. Shigella Isolation & conformation by biochemical tests and serotyping.
- Antibiotics is recommended.. ciprofloxacin, doxycycline, cotrimoxazole .. Shorten the diarrhea duration.... Rehydration is important but not enough..
- Most person develop **non-protective specific** antibodies.. **No healthy carrier stage** .
- Prevention: hygiene.. control of water, milk, fresh food.

# Diarrheagenic *E. coli*-1

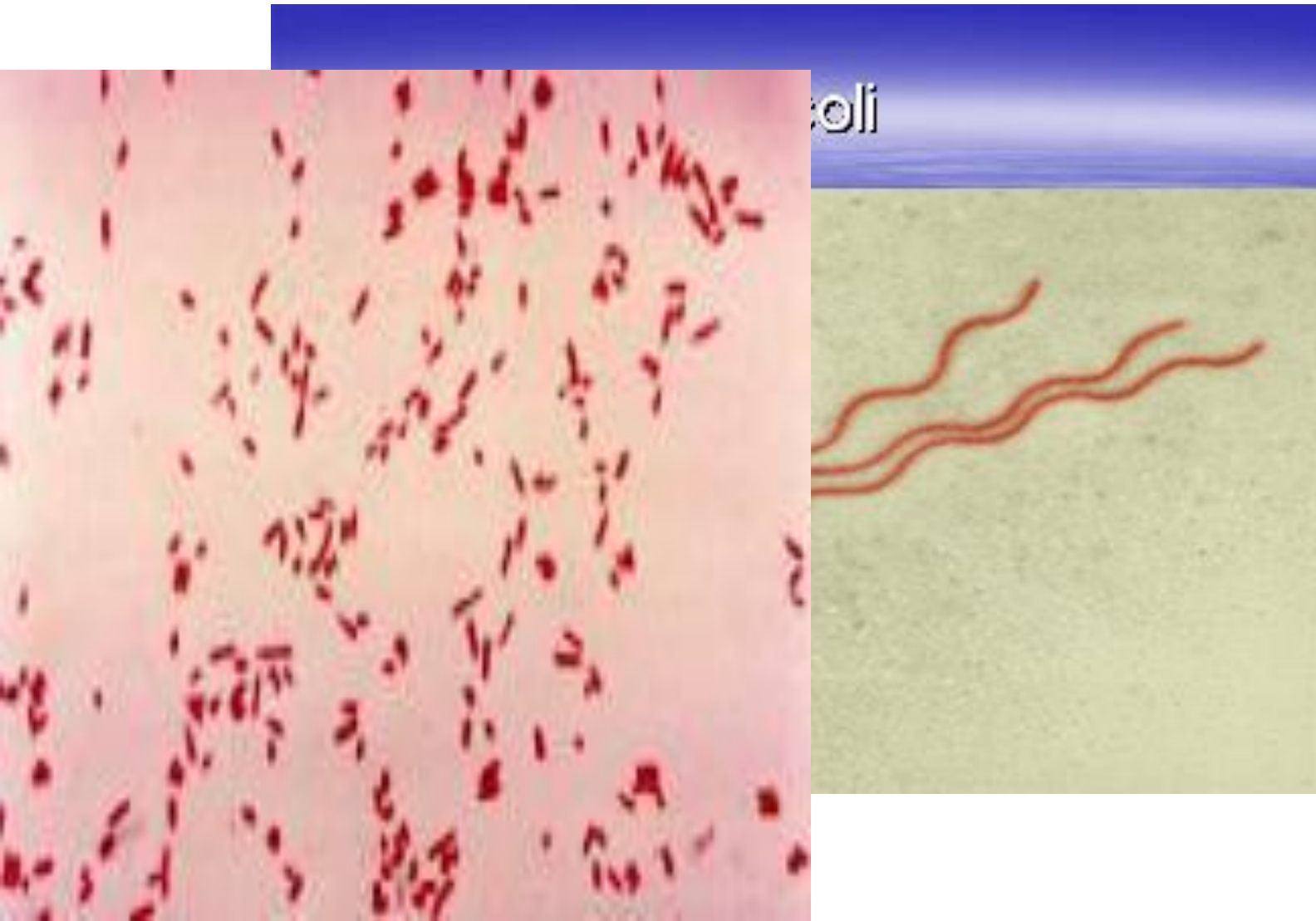
- There are **6 groups of diarrheagenic *E. coli* strains** 5-30%..causing human diarrhea..Widely distributed in water, animals & Birds.. **4 most important types**

**1-Enterotoxigenic *E. coli* (ETEC)**. Common in domestic animals, Poultry, Humans ..Produces Heat stable/ Heat - labile enterotoxins (ST+ LT) or both (plasmid borne).. fimbrial adhesins attached to enterocytes of the small intestine epithelium.

- **LT**.. Similar to cholera toxin, attached to GM1 Ganglioside ..releases & activates adenyl cyclase & increases cellular **cAMP release** .
- **ST** .. activates cGMP.. Both cause prolonged hyper secretion of water & sodium + chloride ions.. Inhibit reabsorption of sodium.. Mild/severe watery diarrhea, vomiting, abdominal pain.. No fever.. 24 hours

# E. Coli Mucosal Attachment and Adhesions by Fimbriae

CFA I & CFA II strains



# Diarrheagenic *E. coli*-2

- **ETEC strains** are common & important cause of diarrhea in infants/very young children .. common cause of **Traveler's diarrhea** in developed countries.
- Contaminated water, Dairy products, fresh vegetable food.
- Self- limited with oral rehydration.. Infection develop intestinal immunity.. Antibiotics are rarely needed,
- 2- **Enterohaemorrhagic *E. coli*** (EHEC) Shiga-like toxin / Vero-toxin..Many serotype strains, commonly **O157: H7** , common in intestines of animals/ cows.. contamination milk & ground beef meat.. causes outbreaks of gastroenteritis. **Complications:** Severe inflammation & ulceration in colon..bloody diarrhea.

# Diarrheagenic E. coli-3

- Haemorrhagic colitis.. If toxin reached blood & Kidneys results Haemolytic Uraemic Syndrome (HUS).. More severe in children/old patients.. Release Blood+ Protein in urine.. Kidney failure.. highly fatal.
- Prevention is better than treatment with antimicrobials.
- 3-Enteropathogenic E.coli (EPEC).. K, LPS Antigens adherence to GI epithelium & distortion.. numerous serotypes.. Common infection in neonates.. Outbreaks watery diarrhea & vomiting in infant nurseries aged less 6 months.. Associated Chronic diarrhea.
- 4-Enteroinvasive E.coli (EIEC).. Similar to Shigella causes bloody diarrhea, Vomiting, Abdominal pain, Fever.. by invasion of damaging intestinal epithelial cells.. necrosis.. Affect all ages..more common and severe in children.

# Lab Diagnosis

- **Detection of Diarrheagenic E. coli strains** in the laboratory is difficult.. complicated by the fact that non-virulent and virulent **E. coli strains** are present in the feces.
- Stool culture on MaConkey agar.. Identification by **PCR more accurate than biochemical and serotyping..**
- Antibiotic treatment is recommended in severe & chronic cases.. Ciprofloxacin, Co-trimoxazole is used for drug-sensitive strains.. second-generation or third-generation cephalosporin for systemic complications.
- **No vaccines are available for all diarrheagenic E.coli**

# Campylobacter

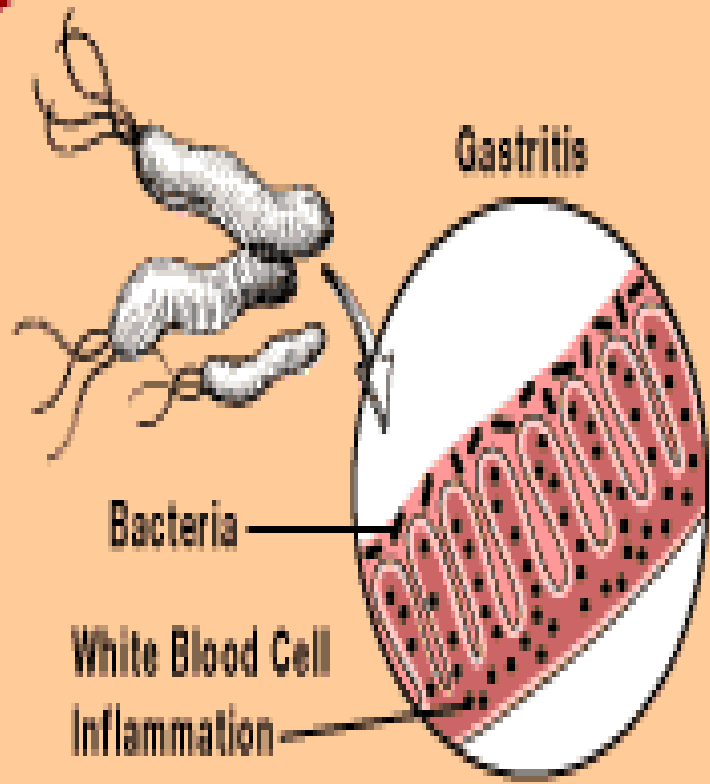
- ***Campylobacter spp.*** are Microaerophilic, Gram-negative, Spiral shape.. Bipolar flagella.. Motile.. Isolation on selective special agar including antibiotics.. at 42 C.
- Commonly present in the GIT of **domestic animals.. poultry & pets** .. Contaminate easily Meat, Dairy products, fresh Food & Direct contact with animals.. Common cause of diarrhea in Western countries.. Less in Arab countries.
- ***Campylobacter jejuni***: Release **various enterotoxin & cytotoxins**.. Acute enteritis, Bloody diarrhea, few days, Infants, children..less adults.. Rarely septicemia in immunodeficiency, Reactive arthritis followed chronic diarrhea.
- Infection mostly self-limited without treatment.
- ***C. fetus***: Less common cause human diarrhea .. Commonly causes sepsis & abortion in animals.
- **Treatment**: Macrolides/Azithromycin, Ciprofloxacin, Ampicillin

# Helicobacter pylori

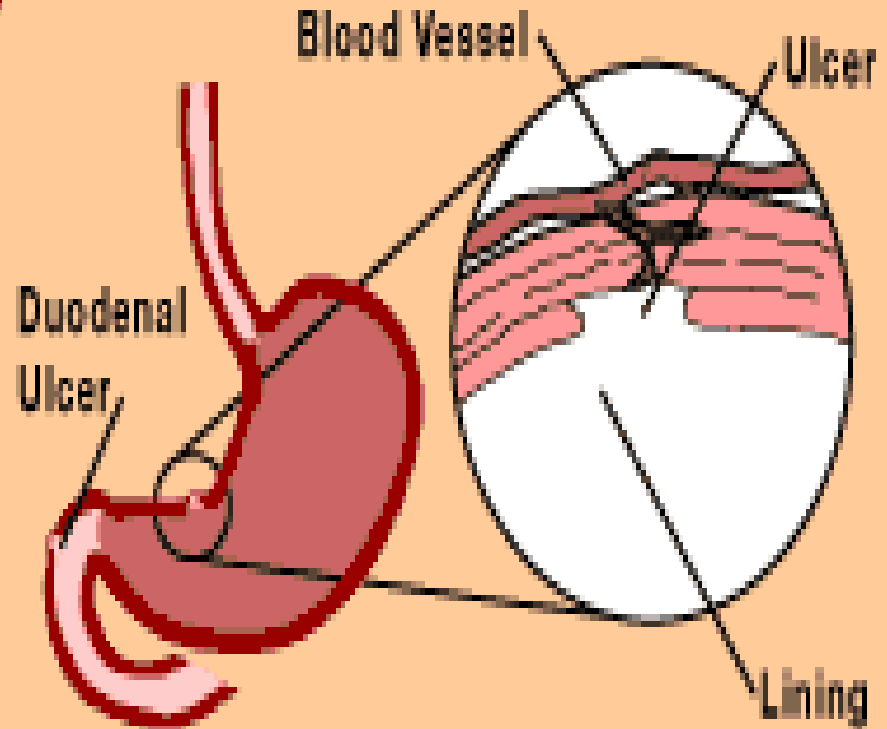
- Microaerophilic growth.. Gram-negative spiral shape, motile, polar 4-6 flagella .. produces potent **urease**, neutralize stomach acidity, allow colonizing mucus overlaying gastric mucosa mainly gastric antrum.
- *H. pylori* colonize stomach of **30%-90%** of world's population according to their age.. Mostly without signs or symptoms and may not cause any disease.
- **Pathogenicity:** Protease, outer membrane antigens & Cytotoxins causing chronic inflammation of the inner lining of the stomach mucosa.. Gastritis, Peptic /duodenal ulcers..about 2 % infected persons.
- *H. pylori* discovered 1983 as cause of chronic gastritis.. Complications Gastric lymphoma, Stomach cancer in infected persons over a long period.



# Helicobacter infection



**Helicobacter Pylori Bacteria**



**Gastric Ulcer**

# Diagnosis & Treatment

- Infection is most likely acquired by ingesting food, water, personal/family contact. Re-infection is common. Optimal growth..selective culture medium with 90%  $\text{CO}_2$  , 42 C, 3-5 days.
- **Diagnoses:** A) clinically **Urea breath test** , using urea capsule labeled with active carbon detects urease activity in stomach by splitting urea into  **$\text{CO}_2$  & Ammonia**. B) A rapid urease test for identification *H. pylori* in gastric biopsy taken by endoscope or **culture**  
& **Giemsa /silver stain** by histological examination.  
Serological antibodies test is less significant.
- **Treatment:** Metronidazole + Clarithromycin / Bismuth sulfate or Metronidazole + Amoxicillin +  $\text{H}_2$  Blockers..

# Vibrios-1

- **Vibrio group** is Gram-negative straight or curved rods, oxidase-positive, motile, single polar flagellum.. Common in sea water/fresh water.
- Classical *V. cholerae* (serotypes 01), 0139 El-tor type.. Infect only human.. Cause Epidemic/Pandemic Outbreaks.. Mostly spread from India subcontinent.
- Noninvasive.. affecting small intestine through Heat-labile Cholera Toxin (A and B subunits) B-unit binds to Gangliosies release A-unit.. Increasing cAMP causing outpouring large amount water,  $\text{Na}^+$ ,  $\text{K}^+$ ,  $\text{Cl}^-$ ,  $\text{HCO}^-$  . Incub. 8-24h..Severe watery diarrhea (1-3 Liters) ,vomiting & cramps, rapid dehydration, blood acidosis, shock, renal failure.. death within 24 h if patient not received replacement of fluid loss .
- **Partial intestinal immunity**.. **antitoxin antibodies** last for 1-year, Oral vaccine is effective for short period.

# Vibrios-2

- Non-O1 V. cholerae.. found in water along with O-1 V.cholerae Less virulent.. watery diarrhea similar to classical cholera due to release cytotoxins.
- V. parahaemolyticus.. Halophilic Vibrio.. Cytotoxins Contaminate raw fish.. cause Gastroenteritis, blood sepsis / Wound infection.
- \* Lab Diagnosis: Stool culture.. All vibrios grow on TCBS.. Identification biochemical & serotyping with specific *V.cholera* antisera.
- \* Treatment: Oral rehydration is the main treatment.. Replacement of fluid loss..doxycycline, cotrimoxazole (children), ciprofloxacin reduce the Vibrios excretion
- \* Prevention: Safe water & Food.. Early detection of positive infected cases prevent outbreak of cholera in community..No Healthy carriers.

# Foodborne Toxigenic Bacteria-1

- **Staphylococcus aureus** strains found in Nose & Skin humans (25%) produce several **Heat-stable exotoxins** (20 minutes 100C) in food at temperature (20-40C).. Fast absorbed from small Intestine to Blood stream & affects CNS. Staphylococcal food poisoning is commonly associated with salty foods, cream cakes, grounded meat.. Fresh dairy products. White chesses. Incub. Period, 30 minutes-6 hours following the consumption of the contaminated food..
- **Main Symptoms**: vomiting, nausea, stomach cramps.. rarely watery diarrhea.. No fever & recovery within 1-2 days.. Self-limited.
- **Lab. Diagnoses**: Detection toxins in food/blood

# Foodborne Toxigenic Bacteria-2

***Bacillus cereus***.. G+ve Aerobic Spore-Forming Bacilli, Common in Nature.. Spores in Food survive boiling and cooling/refrigeration.. Various **exotoxins/ enterotoxins** produced during bacilli sporulation either in Food or Intestine.. Associated with two main gastrointestinal symptoms.

- **1-Intoxication** .. Heat-acid stable **Emetic Enterotoxins** .. Typically developed within 1-24 hours of eating contaminated fried rice, meat.. Vomiting, nausea, stomach cramps last for few hours, No diarrhea or fever. **2- Diarrheal Toxins/ HL**.. mild watery diarrhea, No Fever or Vomiting..self-limiting within 1-3 days.
- Both Types of toxins may produce from the same **B. cereus strain**.. Mostly outbreaks in family, schools & commonly associated with Chinese food.. Fried rice

# Foodborne Toxigenic Bacteria-3

- *Clostridium perfringens*.. G+ve Anaerobic spore-forming ..Widely distributed in the environment.. Common Intestines of humans and animals.. Produce Various **Enterotoxins, Cytotoxins**
- *C. perfringens* toxin-type A ..released in Food at room temperature ..intoxication after 8-24 Hrs.. Diarrhea.. Nausea.. Abdominal Pain.. Rare ly vomiting.. No Fever.. Mostly Self-limited.. 1-2 Days.. No Antibiotic
- *C. perfringens* toxin-Type C.. Released following multiplication in intestine.. severe watery-bloody diarrhea.. **Necrotizing Enteritis**.. No vomiting.. Rarely blood sepsis.. can be fatal in certain patients. Antibiotic treatment is recommended.
- Detection toxin in blood or Food specimens.

# Foodborne Toxigenic Bacteria-4

- *Clostridium botulinum* G+ve Anaerobic Spore-Forming Botulism.. Food-Intoxication.. Incubation 1-24 hrs.
- Consumption improperly or inadequately processed canned food.. meat & fish. Spores develop vegetative growing cells.. Release highly potent **heat-stable neurotoxin ( A-G types)**.. requires 30 min boiling to be inactivated..causing Botulism.
- **Botulinum extotoxin** binds to presynaptic nerve ending of peripheral & cranial nerves.. Interfere with neural transmission by blocking the release of **acetylcholine** .. Flaccid paralysis, Respiratory- Cardiac failure & Death.. Early specific antitoxin may help. Diagnosis: clinical features, detection toxin in food/blood.



# Other Bacteria species

- *Yersinia enterocolitica* ..Gram-ve bacilli, common in contaminated water. Bacteria found intestine of pigs, dogs, cats, other animals. Contaminate often **dairy products** infect mostly children & compromised host .
- Enterocolitis due to cytotoxins..watery-bloody diarrhea & fever, abdominal pain, complications such as skin rash, joint pains or blood sepsis can occur in compromised patients.  
**Treatment:** Trimethoprim-sulfamethoxazole, fluoroquinolones
- *Aeromonas species*.. Gram-ve bacilli, common in natural water sources.. a significant cause of bacterial **gastroenteritis** in association with fish food .. cytotoxins .. young children.. watery diarrhea.. dehydration.. Less Fever & vomiting.

# *Clostridium difficile*

- Anaerobic, spore-forming Gram+ve, Part of normal intestinal flora of neonates- infants & adults (5-20%).. Rapidly increased colonization in hospitalized patients & become actively dangerous after **antibiotic treatment** for more than 1 week with all wide-spectrum penicillins, clindamycin cephalosporins.. Often causes nosocomial infection ( 5-15%) among elderly, surgery & compromised patients.
- **Antibiotic-associated enterocolitis** developed by release **2 toxins types (Enterotoxin A, Cytotoxin B)** acting directly on intestinal epithelial cells causing necrosis.. Bloody diarrhea.. Increased rapidly within days to severe **Pseudomembranous colitis**.. A new strain producing more potent **Binary enterotoxin** detected few years ago.  
**Treatment:** stop use potential causative antibiotics, treatment metronidazole / vancomycin will prevent disease complication.