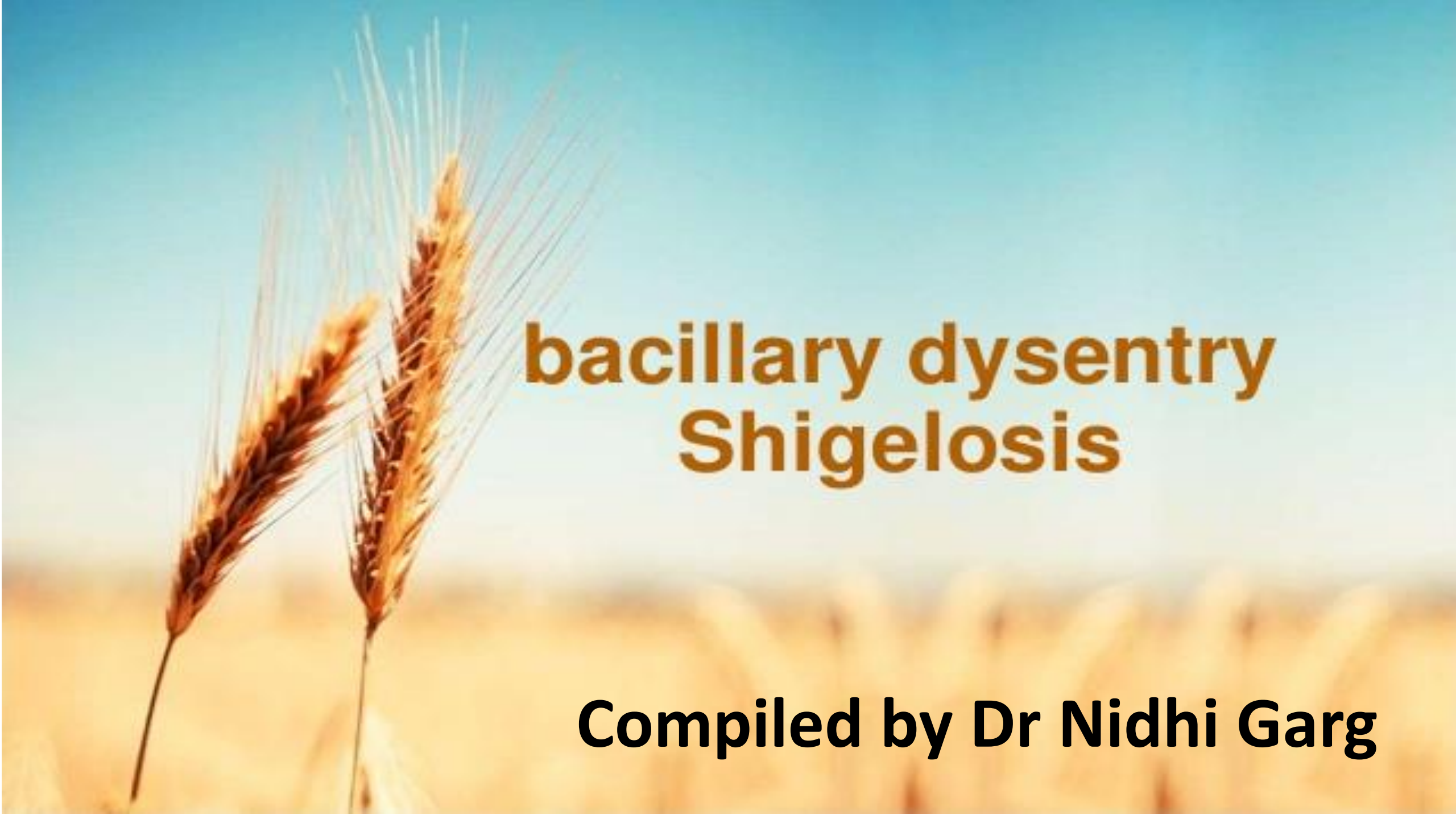


Compiled by Dr Nidhi Garg

WHAT IS DYSENTERY?

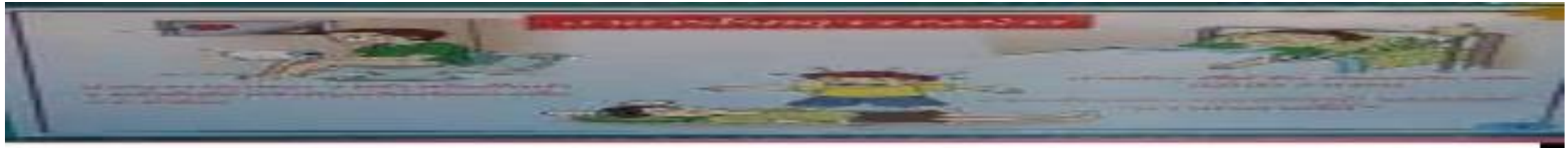
- **Dysentery (formerly known as flux or the bloody flux) broadly refers to::-**
  - Gastrointestinal disorders characterized by inflammation of the intestines, chiefly the colon.
- **The World Health Organization (WHO) defines::-**
  - Dysentery as any episode of diarrhea in which blood is present in loose, watery stools.

WHAT CAUSES DYSENTERY?

- **The bacteria *Shigella* and *E coli* and the amoeba *Entamoeba histolytica* are the most common causes of dysentery. These organisms are present in the stool (feces) of infected people and animals.**
- **The *Entamoeba histolytica* may uneventfully reside in the colon, but if it attacks the colon wall, it can cause dysentery.**
- **People with weakened immune systems are also more likely to develop amoebic dysentery.**
- **Most commonly, dysentery is caused by drinking water or eating food from sources contaminated with feces containing the pathogens.**
- **Swimming in contaminated water may also result in dysentery.**
  - For this reason, dysentery occurs most frequently in people traveling to developing countries and in children who touch infected human or animal feces without proper hand washing.

COMMON CAUSES OF DYSENTERY

- **Several organisms are known to cause dysentery, most commonly:**
  - *Campylobacter*
  - Certain types of *E coli*
  - *Entamoeba histolytica*
  - *Salmonella*
  - *Shigella*
- **Dysentery is also spread through food that has been contaminated with human faeces (stools), particularly cold, uncooked food, such as salad.**
- **This is more likely to happen in countries where:**
  - There is poor sanitation
  - Water supplies and sewage disposal are inadequate
  - Human faeces are used as fertilizer
- **Severe dysentery is more common in developing countries.**
- **The time between coming into contact with the bacteria and the symptoms starting (the incubation period) is usually** one to seven days.



BACILLARY DYSENTERY

- Bacillary dysentery (shigellosis) is caused by shigella bacteria.
- The shigella bacteria are found in faeces and are spread through poor hygiene; for example, by not washing your hands after having diarrhea.
- If you do not wash your hands, you can transfer the bacteria to other surfaces. The bacteria can then infect someone else if they touch the surface and transfer the bacteria to their mouth. The bacteria will travel from the mouth to the bowel, invading the cells that line the large bowel. The bacteria multiply, killing the cells and producing the symptoms of dysentery.
- In the **India**, most cases of bacillary dysentery are spread within families and in places where people are in close contact with one another, such as in schools, nurseries, military bases and day centers. The condition can be spread for up to four weeks after a person has become infected.

Causative agent

- Shigella strains are gram negative , faculatively anaerobic,non motile rods classified in the family enterobacteriacae.
- Shigella strains cause dysentry by invading and destroying the cells that line the large intestine
- There are 4 subgroups of shigella
  - Group A: S.dysenteriae (most severe infection due to shig toxin type 1)
  - Group B: S.flexneri
  - Group C: S.bodyii
  - Group D: s.sonni
- Group A<B<C are further subdivided into 15,8,19 serotype respectively. While group D consist of a single serotype

epidmiology

- Shigellosis causes an estimated 150 million illnesses and 14,000 deathes worldwide
- Its endemic in both tropical & temprate climate
- *S. dysenteriae* type 1 is of particular concern in developing countries and complex emergency situations where huge outbreaks can occur.
- *S. sonnei* is most common in industrialized countries, where the disease is generally less severe

Epidemiology

- Shigellosis is a major cause of diarrheal disease (developing nations)
- Major cause of bacillary dysentery (severe second stage form of shigellosis)
- Leading cause of infant diarrhea and mortality (death) in developing countries

Shigellosis and Endemicity

- Shigellosis is endemic in developing countries were sanitation is poor. Typically 10 to 20 percent of enteric disease, and 50% of the bloody diarrhea or dysentery of young children, can be characterized as shigellosis, and the prevalence of these infections decreases significantly after five years of life.

Developed countries too Suffer Shigella Infections

- In developed countries, single-source, food or water-borne outbreaks occur sporadically, and pockets of endemic shigellosis can be found in institutions and in remote areas with substandard sanitary facilities.

Period of communicability

- During acute infection and until the infectious agent is no longer present in feces, usually within 4 weeks after illness.
- Asymptomatic carriers may transmit infection; rarely, the carrier state may persist for months or longer.
- Appropriate antimicrobial treatment usually reduces duration of carriage to a few days.

Shigella a Highly Infectious Bacteria

- *Shigella* is one of the most infectious of bacteria and ingestion of as few as **100-200 organisms** will cause disease.
- Most individuals are infected with shigellae when they ingest food or water contaminated with human fecal material.
- Shigella can survive up to 30 days in milk, eggs, cheese or shrimps.

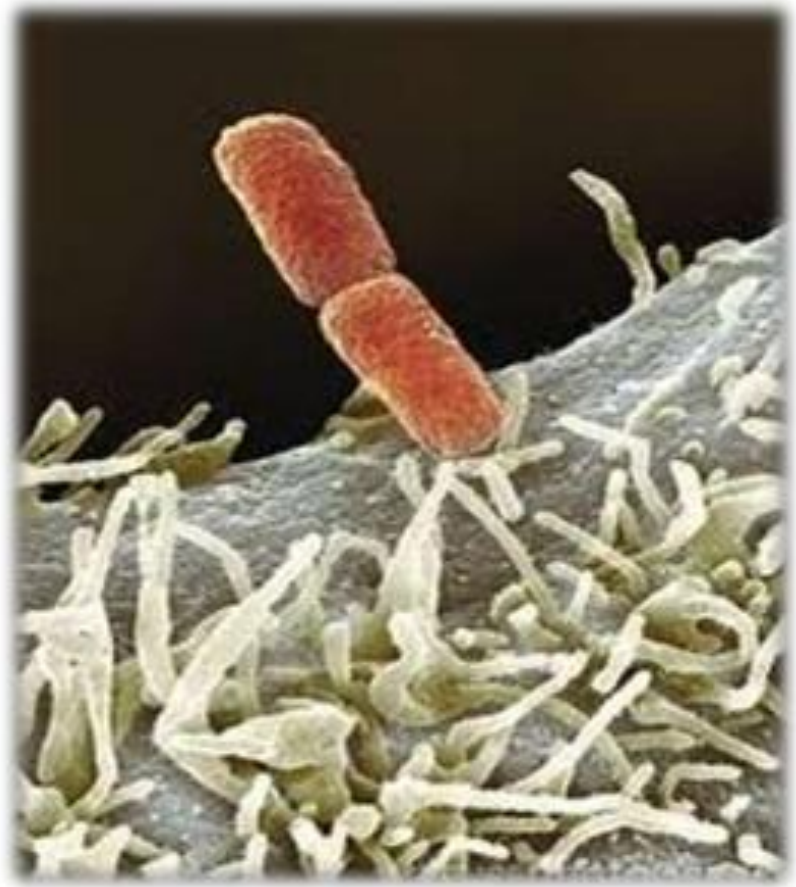
Morphology & Physiology

- Small Gram-negative, facultatively anaerobic, coliform bacillus
- Non-motile (no H antigen)
- Possess capsule (K antigen) and O antigen
- **K antigen** not useful in serologic typing, but can interfere with O antigen determination
- **O antigens**: A, B, C, D correspond respectively to the four species
- Non-lactose fermenting
- Bile salts resistant: trait useful for selective media

ferment glucose

Reduce nitrates (NO_3 to NO_2 or N_2)

are oxidase negative



Taxonomy

Family *Enterobacteriaceae*

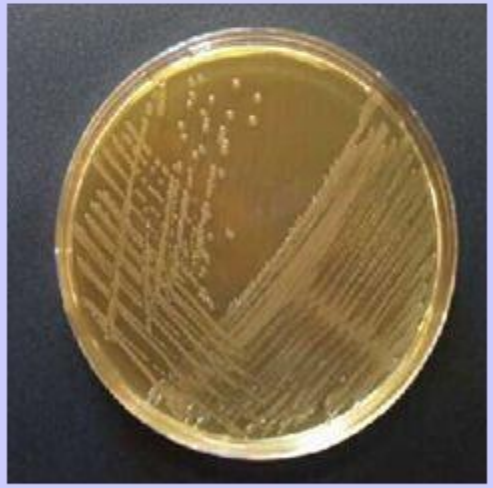
1. ***Shigella dysenteriae***: most serious form of bacillary dysentery
2. ***Shigella flexneri***: shigellosis in underdeveloped countries
3. ***Shigella sonnei***: shigellosis in developed countries
4. ***Shigella boydii***

CLASSIFICATION
on Basis of Mannitol Fermentation:

- 1. Non-mannitol-fermenters
- *Shigella dysenteria*
- 2. Mannitol-fermenters
- *Shigella flexneri*
- *Shigella boydii*
- *Shigella sonnei*

Shigella spp Isolation

- *Shigella* organisms may be very difficult to distinguish biochemically from *Escherichia coli.*
- *Shigella* species are Gram-negative, facultatively anaerobic, nonsporulating, nonmotile rods in the family *Enterobacteriaceae*.
- They do not decarboxylate lysine or ferment lactose within 2 days.



NON-LACTOSE FERMENTERS: COLOURLESS COLONIES

MacConkey Agar
LACTOSE FERMENTERS: RED/PINK COLONIES

CULTURAL CHARACTERISTICS

- All members of Shigella are aerobic and facultative anaerobes.
- Grow readily in culture media at pH 6.4 to 7.8 at 10 oC - 40 oC, with optimum of 37 oC.
- After 24 hours incubation, Shigella colonies reaches a diameter of about 2 mm.
- The colonies are circular, convex, colorless, but moderately translucent with smooth surface, and entire edges.

Growth on Selective Medium

In XLD they appear pinkish to reddish colonies while in Heaktoen Enteric Agar (HEA), they give green to blue green colonies.

HABITAT AND TRANSMISSION

- Shigella species are found only in the human intestinal tract.
- Carriers of pathogenic strains can excrete the organism up to two weeks after infection and occasionally for longer periods.
- Shigella are killed by drying. Shigella are transmitted by the fecal-oral rout.
- The highest incidence of Shigellosis occur in areas of poor sanitation and where water supplies are polluted.

Factors Contributing Spread

- Spread is always from **a human resource** and generally involves one of the five *f*'s:
  - **food,**
  - **fingers,**
  - **feces,**
  - **flies or**
  - **fomites.**
- This is in contrast to salmonellae, which are often spread to humans from infected animals.

PATHOGENESIS

- SOURCE : MAN: CASE OR CARRIER
- MODE OF SPREAD: CONTAMINATED FINGERS, FOOD, FLIES, FOMITES
- PERSON TO PERSON TRANSMISSION
- INFECTIVE DOSE: 10-100 VIABLE BACILLI
- HIGHEST CONCENTRATION IN STOOL DURING EARLY/ACUTE INFECTION 10^3 TO 10^9 VIABLE BACILLI PER GRAM OF STOOL
- POST CONVALESCENT SHEDDING : LOW COUNTS 10^2 TO 10^3

Transmission

- Faecal-oral transmission is the main path of Shigella infection. Other modes of transmission include ingestion of contaminated food or water, contact with infected objects, or sexual contact. Outbreaks of Shigella infection are common in places where sanitation is poor.

PATHOGENIC DETERMINANTS

O antigen: The ability to survive the passage through the host defenses may be due to O antigen.

Invasiveness: Virulent Shigella penetrate the mucosa and epithelial cells of the colon in an uneven manner. Intracellular multiplication leads to invasion of adjacent cells, inflammation and cell death. Cell death is probably due to cytotoxic properties of shiga toxin that interfere with protein synthesis. The cellular death and resulting phagocytosis response by the host accounts for the bloody discharge of mucus and pus and shallow ulcers characteristic of the disease.

Other toxins: It has a protein toxin which may be neurotoxic, cytotoxic, and enterotoxic. The enterotoxic property is responsible for watery diarrhea.

PATHOGENICITY

Shigella dysentery's form a powerful exotoxin, it is associated with epidemics of bacillary dysentery.

In man, shigellosis begins with symptoms of acute gastro-enteritis which is accompanied by abdominal pain and diarrhea.

As it progresses, diarrhea becomes more frequent and is usually accompanied colicky pain.

PATHOGENICITY

- Later diarrhea losses its fecal characteristic and is followed by mucus with pus and blood.
- The disease is usually accompanied by fever and marked prostration. It is also known that children are more frequently attacked than adult persons and the symptoms are more severe.

Pathogenesis and Virulence Factors (cont.)

Invasiveness in *Shigella*-Associated Dysentery

- Penetrate through mucosal surface of colon (colonic mucosa) and invade and multiply in the colonic epithelium but do not typically invade beyond the epithelium into the lamina propria (thin layer of fibrous connective tissue immediately beneath the surface epithelium of mucous membranes)
- Preferentially attach to and invade into M cells in Peyer's patches (lymphoid tissue, i.e., lymphatic system) of small intestine

Invasiveness in *Shigella*-Associated Dysentery (cont.)

- M cells typically transport foreign antigens from the intestine to underlying macrophages, but *Shigella* can lyse the phagocytic vacuole (phagosome) and replicate in the cytoplasm
  - Note: This contrasts with *Salmonella* which multiplies in the phagocytic vacuole
- Actin filaments propel the bacteria through the cytoplasm and into adjacent epithelial cells with cell-to-cell passage, thereby effectively avoiding antibody-mediated humoral immunity (similar to *Listeria monocytogenes*)

Pathogenesis and Virulence Factors (cont.)

Shiga Toxin Effects in Shigellosis

Enterotoxic Effect:

- Adheres to small intestine receptors
- Blocks absorption (uptake) of electrolytes, glucose, and amino acids from the intestinal lumen
  - Note: This contrasts with the effects of cholera toxin (*Vibrio cholerae*) and labile toxin (LT) of enterotoxigenic *E. coli* (ETEC) which act by blocking absorption of Na^+, but also cause hypersecretion of water and ions of Cl^-, K^+ (low potassium = hypokalemia), and HCO_3^- (loss of bicarbonate buffering capacity leads to metabolic acidosis) out of the intestine and into the lumen

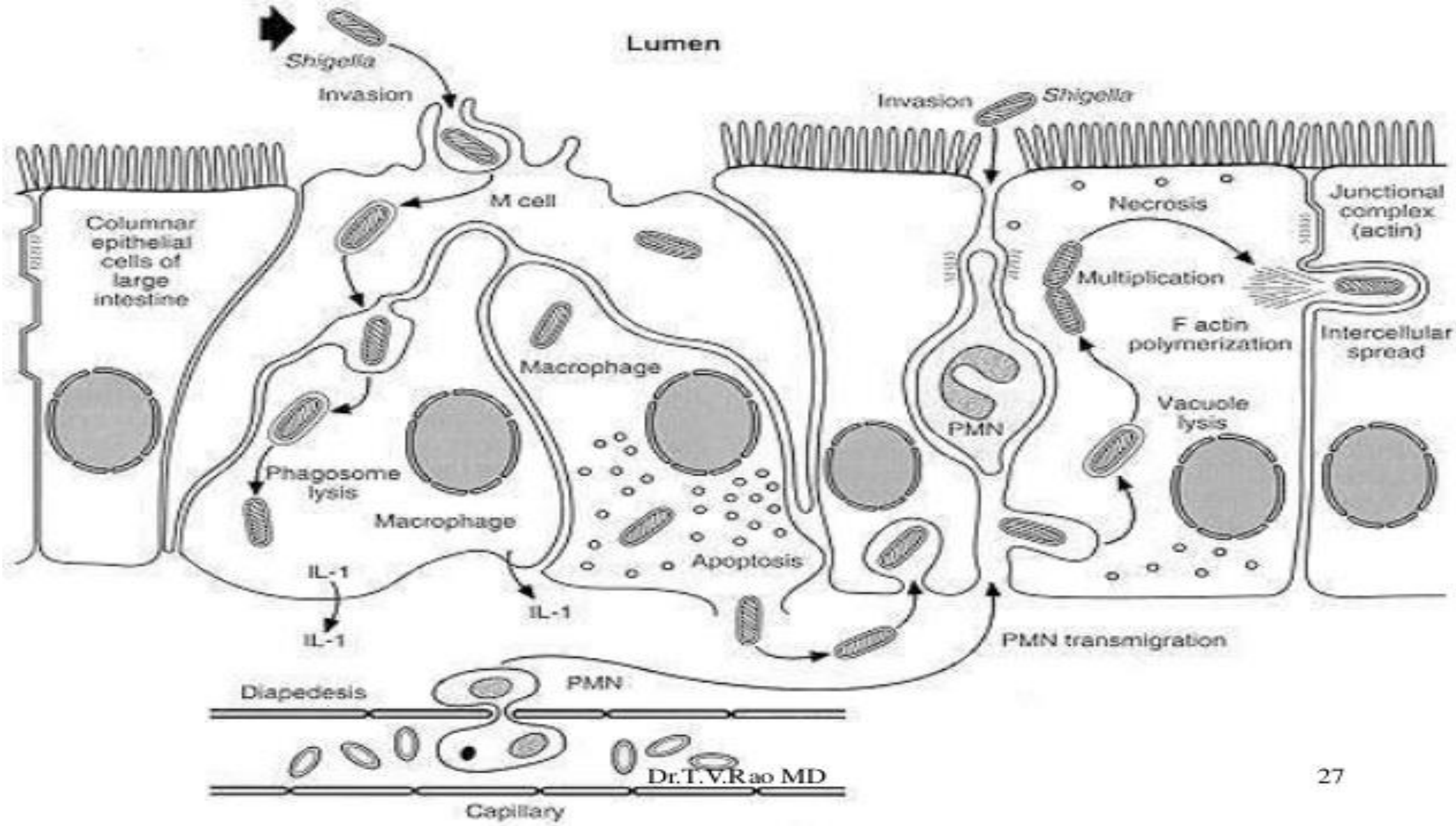
Pathogenesis and Virulence Factors (cont.)

Shiga Toxin Effects in Shigellosis (cont.)

Cytotoxic Effect:

- B subunit of Shiga toxin binds host cell glycolipid
- A domain is internalized via receptor-mediated endocytosis (coated pits)
- Causes irreversible inactivation of the 60S ribosomal subunit, thereby causing:
  - Inhibition of protein synthesis
  - Cell death
  - Microvasculature damage to the intestine
  - Hemorrhage (blood & fecal leukocytes in stool)

Neurotoxic Effect: Fever, abdominal cramping are considered signs of neurotoxicity


Lumen
Shigella
Invasion
M cell
Columnar epithelial cells of large intestine
Macrophage
Phagosome lysis
Macrophage
IL-1
IL-1
IL-1
Apoptosis
Diapedesis
PMN
Capillary
Invasion
Shigella
Necrosis
Junctional complex (actin)
Multiplication
F actin polymerization
Intercellular spread
Vacuole lysis
PMN
PMN transmigration

Characteristics of Shiga Toxin

- Enterotoxic, neurotoxic and cytotoxic
- Encoded by chromosomal genes
- Two domain (A-5B) structure
- Similar to the Shiga-like toxin of enterohemorrhagic *E. coli* (EHEC)
  - NOTE: except that Shiga-like toxin is encoded by lysogenic bacteriophage

SIGNS AND SYMPTOMS OF DYSENTERY

➢ Dysentery causes irritation and inflammation of the intestines that may result in a number of symptoms . The symptoms can vary in intensity among individuals.

Common symptoms of Dysentery

The most common symptoms of dysentery are related to *disturbances of the digestive system* and include:

- ➢ Abdominal bloating
- ➢ Abdominal pain
- ➢ Bloody diarrhea
- ➢ Flatulence
- ➢ Nausea with or without vomiting

OTHER SYMPTOMS OF DYSENTERY

➢ **As the dysentery infection progresses, other symptoms, including *symptoms of dehydration*, may develop.**

➢ **Other possible symptoms include:**

- ❑ Decreased urine output
- ❑ Dry skin and mucous membranes (such as dry mouth)
- ❑ Feeling very thirsty
- ❑ Fever and chills
- ❑ Muscle cramps
- ❑ Muscle weakness (loss of strength)
- ❑ Weight loss

SERIOUS SYMPTOMS THAT MIGHT INDICATE A LIFE-THREATENING CONDITION

➢**On rare occasions, dehydration resulting from dysentery may be so severe that a life-threatening situation can develop.**

The following symptoms:

- ❑Change in level of consciousness or alertness, such as passing out or unresponsiveness
- ❑Change in mental status or sudden behavior change, such as confusion, delirium, lethargy, hallucinations and delusions
- ❑High fever (higher than 101 degrees Fahrenheit)
- ❑Rapid heart rate (tachycardia)
- ❑Severe abdominal pain
- ❑Severe dizziness

Clinical Syndromes (Shigellosis)

- Ranges from asymptomatic infection to severe bacillary dysentery
- **Two-stage disease:** watery diarrhea changing to dysentery with frequent small stools with blood and mucus, tenesmus, cramps, fever

Early stage:

- Watery diarrhea attributed to the enterotoxic activity of Shiga toxin
- Fever attributed to neurotoxic activity of toxin

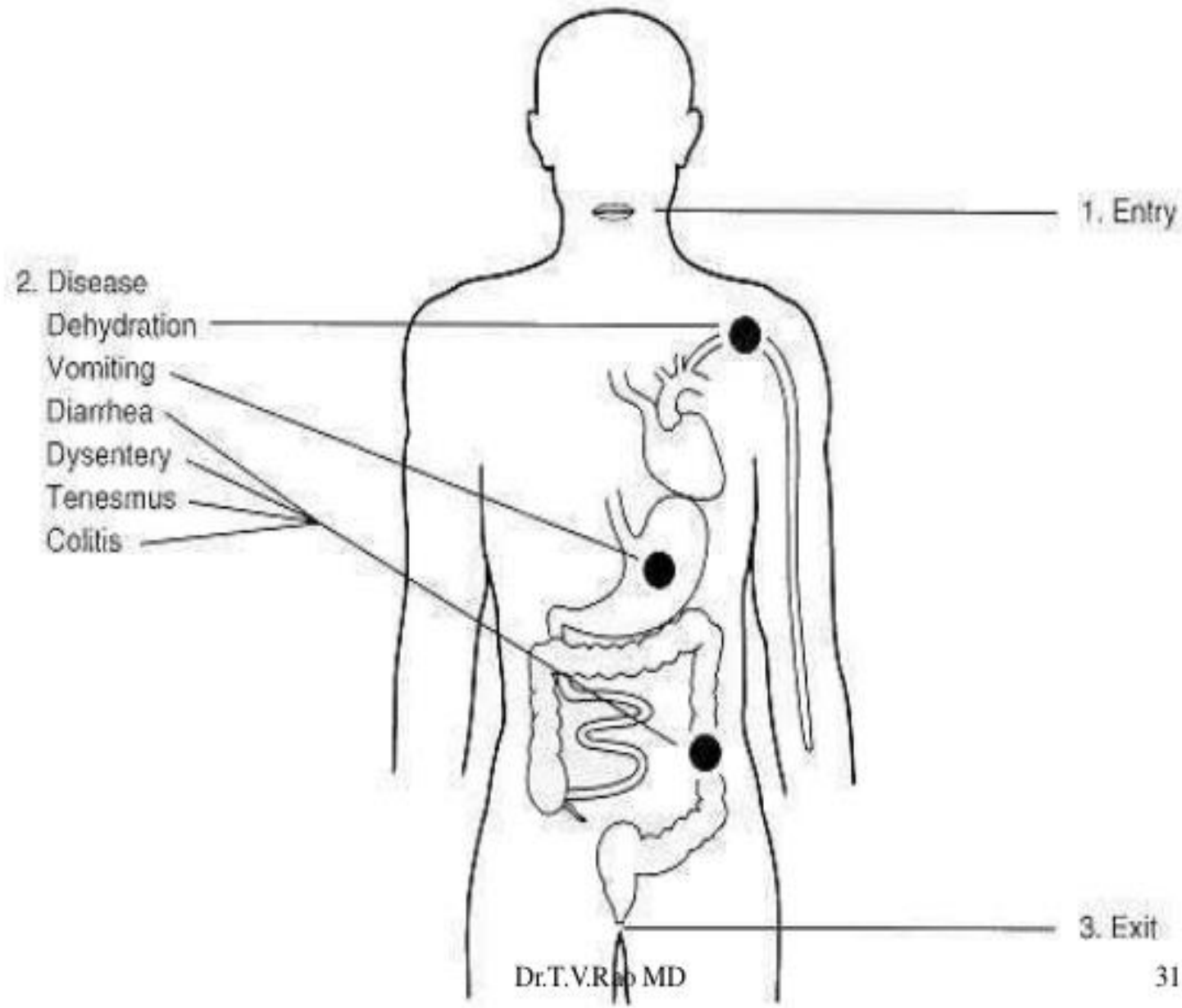
Clinical Syndromes

Process involves:

- ✓ 1. Ingestion
- ✓ 2. Non-invasive colonization and cell multiplication
- 3. Production of the enterotoxin by the pathogenic bacteria in the small intestine;

Second stage:

- Adherence to and tissue invasion of large intestine
- Typical symptoms of dysentery
- Cytotoxic activity of Shiga toxin increases severity


1. Entry
2. Disease
Dehydration
Vomiting
Diarrhea
Dysentery
Tenesmus
Colitis
3. Exit

RISK FACTORS FOR DYSENTERY

A number of factors increase the risk of developing dysentery. Not all people with risk factors will get dysentery.

Risk factors for dysentery include:: -

- **Attendance or work in a day care setting**
- **Close contact with an infected person or animal**
- **Consumption of untreated water from lakes, rivers or streams**
- **Fecal to oral contact**
- **Travel in countries where the infection is common**
- **Use of public swimming pools**

Methods to Diagnose Shigellosis

- Shigellosis can be correctly diagnosed in most patients on the basis of fresh blood in the stool. Neutrophils in fecal smears is also a strongly suggestive sign. Nonetheless, watery, mucoid diarrhea may be the only symptom of many S sonnei infections, and any clinical diagnosis should be confirmed by cultivation of the etiologic agent from stools.

LABORATORY DIAGNOSIS

The only satisfactory method of laboratory diagnosis is to cultivate the bacilli from the patient.

In the early stages of acute shigellosis, isolation of the causative organism from the feces is usually accomplished without difficulties by using the same special media and methods employed for salmonella

Laboratory Identification:

- Closely related to *Escherichia*
- Species (serogrouping and biochemical analysis
- Stool specimens and rectal swabs should be cultured soon after collection or placed in appropriate transport medium **(Cary-Blair medium)**
- **Readily isolated on selective/differential agar media (XLD, SS, and brilliant green agar)**
- Lactose nonfermenter

Processing of Rectal Swabs

- Rectal swabs may also be used to culture Shigella if the specimen is processed rapidly or is deposited in a buffered glycerol saline holding solution. Isolation of Shigella in the clinical laboratory typically involves an initial streaking for isolation on differential/selective media with aerobic incubation to inhibit the growth of the anaerobic normal flora.

Culture Media for Identification

- Commonly used primary isolation media include MacConkey, Hektoen Enteric Agar, and Salmonella-Shigella (SS) Agar. These media contain bile salts to inhibit the growth of other Gram-negative bacteria and pH indicators to differentiate lactose fermenters (Coliforms) from non-lactose fermenters such as Shigella

Shigella on MacConkey
Shigella on SS agar
Shigella on ENDO
Shigella on EMB
Shigella on Hektoen

TREATMENT OF DYSENTERY

➢ Treatment for dysentery begins with seeking medical care from our health care provider.

➢To determine if we have dysentery, our health care provider may ask us to provide stool samples for laboratory testing.

➢ Antibiotic therapy is the mainstay of treatment for dysentery due to bacterial organisms and is highly effective. It is important to follow our treatment plan for dysentery precisely and to take all of the antibiotics as instructed to avoid reinfection or recurrence.

Antibiotics for the treatment of dysentery ::-

- ❑ Ceftriaxone (Rocephin)
- ❑ Ciprofloxacin (Cipro)
- ❑ Trimethoprim-sulfamethoxazole (Bactrim, Septra)

➢ The most common treatment for amebic dysentery caused by *Entamoeba histolytica* is *metronidazole (Flagyl*), an antiparasitic medication.

➢ If we have diarrhea and vomiting, *fluid and electrolyte replenishment* is also a component of successful treatment.

➢ The seed, leaves, and bark of the ***kapok tree*** have been used in traditional medicine by indigenous peoples of the rain forest regions in ***the Americas, West-Central Africa, and South East Asia*** to treat this disease

Case mangment

- Refer seriously ill or severely malnourished patients to hospital immediately.
- Check the results of antimicrobial sensitivity tests with the laboratory.
- Give an antimicrobial effective against local *S. dysenteriae* type 1 (Sd1)strains promptly to all patients, preferably as inpatients
- Treat dehydration with oral rehydration salts or intravenous fluids if severe.
- If the antimicrobials used are effective, clinical improvement should be noted within 48 hours.

Table 5.2 Recommended antibiotics for treatment of *Shigella dysenteriae* type 1

ADULTS: ciprofloxacin	500 mg	twice a day	by mouth for 3 days
CHILDREN: ciprofloxacin	15 mg/kg	twice a day	by mouth for 3 days
FOR CHILDREN AGED UNDER 6 MONTHS: ★ add zinc	zinc 10 mg	daily	by mouth for 2 weeks
FOR CHILDREN AGED 6 MONTHS TO 3 YEARS: add zinc	zinc 20 mg	daily	by mouth for 2 weeks

Children < 6 mo. Less likely to get infected as breast feeding is protective

Note: rapidly evolving antimicrobial resistance is a real problem. Shigella is usually resistant to ampicillin and trimethoprim sulfamethoxazole (TMP-SMX)

- Azithromycin and ceftrixone may also be considered for treatment of shigellosis especially in children
- The use of antimotility agents is discourged as they prolong the duration of illness

Yet No Licenced Vaccine

- Currently, no licensed vaccines targeting Shigella or ETEC exist; however, vaccines against both bacteria are in development.

TIPS TO PREVENT DYSENTERY

- Washing one's hands with an antibacterial soap after using the toilet, the bathroom, changing diapers, after contact with an infected person, and regularly throughout the day.
- Washing one's hands before handling, cooking and eating food, handling babies, and feeding young or elderly people.
- Keeping contact with someone known to have dysentery to a minimum.
- Washing laundry on the hottest setting possible.
- Avoiding sharing items such as towels and face cloths.
- Avoid swallowing water in swimming pools or other recreational water sources
- Make sure you drink only purified water.
- Drink packaged drinking water when travelling.

Mangment of contacts

- Whenever feasible ill contacts should be discouraged from handling food ,caring of children and patients .. Until diareah stop and stool culutre is negative in one or more succesive test taken 24 hours apart and 48 hours after discontinuation of antibiotics
- Thourogh hand washing after defecation, before food handling and caring of children \ patients is essential
- Investigate water and food sources and recreational water sources using general sanitation measures

DYSENTERY

CONCLUSION

- *Nearly ~225,000 children die every year from diarrhea / dysentery accounting for more than a tenth of all childhood deaths*
- *246 mln cases of diarrhea/ dysentery in India / year*
- *Over half of all diarrhea/dysentery patients in India seek treatment from the private sector, but most do not receive the recommended treatment, ORS/Zinc.*
- *Three high burden states are Uttar Pradesh, Madhya Pradesh and Gujarat .*
- *We have to Ensure last mile availability of high quality medicinal treatment.*
- *By strengthening the public and private sector supply chain/distribution systems.*

(Source: World Health Statistics 2011 www.who.int ,District Level Household and Facility Survey 2007-08)

Hand Washing Can Still Save Many from Shigellosis