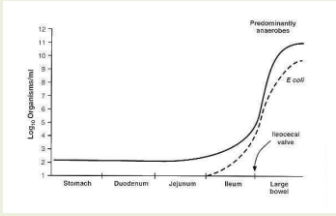
Microbiology of Bowel Infections

Normal enteric microflora

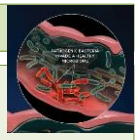
- Over 400 bacterial species
- **Anaerobes** outnumber facultative anaerobes
- The flora is sparse in the stomach and upper intestine, but luxuriant in the **lower bowel**
- Bacteria occur both in the lumen and attached to the mucosa
- **Lactobacillus, Bacteroides, and Clostridium** spp. attach to the intestinal epithelial surface and act synergistically with the host immunity

Normal enteric microflora



Concentration of the bacterial flora in regions of the gastrointestinal tract

Types of enteric infections



- Microbe-host interactions alter normal intestinal physiology **in one of three ways**:

(1) shift in the delicate balance of bidirectional water and electrolyte fluxes in the upper small bowel

by

intraluminal toxins or **minimally invasive organisms**

Types of enteric infections ……

(2) Inflammatory or **cytotoxic destruction** of the ileal or colonic mucosa

Eg : Shigella

Types of enteric infections

(3) **Penetration** through an intact mucosa to the reticuloendothelial system

This usually results in a febrile systemic illness with or without diarrhea.

e.g. ***S. typhi***

Infectious Doses of Enteric Pathogens

Pathogen	Infectious Dose (No. of Organisms)
• *Shigella*	10 to 10^2
• EHEC	Unknown (likely low)
• *Campylobacter jejuni*	10^2 to 10^6
• *Salmonella*	10^5
• Non-EHEC	10^8
• *Vibrio cholerae*	10^8
• *Giardia lamblia*	10 to 10^2 cysts
• *Entamoeba histolytica*	10 to 10^2 cysts
• *Cryptosporidium parvum*	1 to 10^3 oocysts

Microbial Factors

- Toxins
- Attachment
- Invasiveness
- Other virulence factors

Toxins

- Toxic **microbial components** or **products**
- Capable of altering gastrointestinal structure or function in the absence of the organisms themselves.

Enteric Bacterial Toxins

Neurotoxin Group

- *Clostridium botulinum* (botulinum toxins)
- *Staphylococcus aureus* (enterotoxin b)
- *Bacillus cereus* (emetic toxin)

- Usually ingested as **preformed toxins** that often cause enteric symptoms.

Staphylococcal food poisoning

- This occurs when *S. aureus* is inoculated into food which is then **left** in conditions that are permissive for bacterial **multiplication** and **toxin secretion** before consumption.
- Abrupt **upper gastrointestinal** syndrome attributed to staphylococcal **enterotoxin**

Staphylococcal food poisoning….

- Effect is caused by action of **super antigen** (enterotoxin) on the central autonomic nervous system
- Staphylococcal **α-toxin** - elicits **hyperperistalsis**
- Nausea and vomiting occur after an incubation period of **2 and 6 h**

Staphylococcal food poisoning….

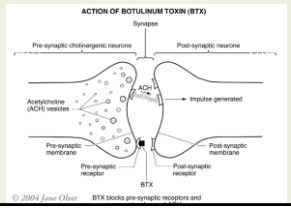
- **Abdominal pain** and **diarrhoea** are also common
- Diagnosis is made on **clinical** grounds.
- Suspected **food** can be **cultured** for the presence of *S. aureus.*

B. cereus - Emetic type

- Highly heat-stable emetic toxin (especially when cultured with **rice**)
- Characterized by a **shorter onset** period of **1–6 h**, and the symptoms resemble those of *S. aureus* food poisoning.
- Nausea, vomiting and malaise, occasionally with diarrhea
- Recovery within 24 h is usual

Botulinum toxin

Primary effect on the **neuromuscular junction** **prevent the release of acetylcholine** from the presynaptic vesicle.



Secretory Enterotoxin group

- *Vibrio cholerae* (cAMP)
- Noncholera vibrios
- *Escherichia coli*, LT (cAMP)
- *E. coli*, STa (cGMP)
- *E. coli*, STb
- *Salmonella*
- *Klebsiella*
- *Clostridium perfringens* (A)
- *Shigella dysenteriae*
- *B. cereus*

B. cereus - diarrheal type

- Has **long incubation** as **8–16** h, followed by abdominal cramps, profuse watery **diarrhoea** and rectal tenesmus.
- Occasionally -fever and vomiting.

Cytotoxin Group

- ***Shigella***
- *C. perfringens* (A)
- *Vibrio parahaemolyticus*
- *Clostridium difficile* (A and B)
- *E. coli* (EHEC)
- *Campylobacter jejuni*
- *Helicobacter pylori*
- *Bacteroides fragilis*

Shigella

- Causes dysentery
- No toxaemia
- IBP- 2–3 days
- Clinical features vary markedly among the different types

  Shigella sonnei – mildest illness.

  S. flexneri and *S. dysenteriae* may develop blood and mucus diarrhoea
- Abdominal pain & tenderness are frequent

Enterotoxins

- Has a direct effect on the intestinal mucosa to elicit **net fluid secretion**

  E.g. **Cholera toxin**

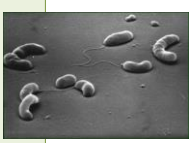
  causes fluid secretion after B subunit bind & releases the A2 toxin subunit that **activate adenylate cyclase** & leads to increase concentrations of intestinal **cAMP.**

  In addition, **prostaglandins, platelet-activating factor** and **serotonin** involve in secretory response to cholera toxin.

Cholera – Rice water stool

Cholera

- **Diverse presentation** with many asymptomatic cases and others with severe symptoms.
- IBP - 1 to 5 days
- Sudden onset of symptoms and rapidly progressive.
- Diarrhoea is severe
- Fatal - **dehydration** with loss of water and salts
- **Abdominal pain** is usually **absent**
- Vomiting - in the early stages



Enterotoxins

- ***E. coli:*** Produce heat-labile enterotoxin (LT)
- ***Klebsiella***
- ***Citrobacter***
- ***Salmonella***
- ***C. jejuni***

  Produce cholera-like heat-labile toxin

Associated with **watery diarrhea**

Salmonellosis

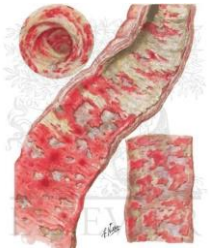
- Symptoms develop **within 24 h** after ingestion of the organisms.
- Develop nausea, vomiting and diarrhoea.
- Fever and abdominal pain are also common
- After symptoms subside patients **continue to excrete organisms** in their stools for up to 3 months.
- Approximately 1–3% may excrete organisms for more than a year.

Cytotoxins and Mixed Toxins

- Causes **mucosal destruction**
- Results **inflammatory colitis.**

e.g. - Shiga toxin from *S. dysenteriae* type 1

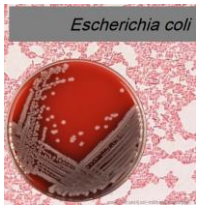
Causes colonic mucosal destruction in bacillary dysentery



Cytotoxins and Mixed Toxins

E. coli

- Shiga-like toxins (SLT)- more pronounced in EHEC
- Toxins, known as SLT-1 and SLT-2 in *E. coli* O157:H7.
- *E. coli* SLT-1 has **binding** and **active subunits** which **halt protein synthesis**
- Complicated with hemorrhagic colitis or the hemolytic-uremic syndrome



Cytotoxins and Mixed Toxins

- *Clostridium perfringens*

C. perfringens enterotoxin produces cytotoxicity **similar to that of *S. dysenteriae*** toxin

Cytotoxins and Mixed Toxins

- *V. parahaemolyticus*

cause of seafood-borne **diarrheal illness** outbreaks

Toxin - thermostable

hemolysin

cytotoxic

enterotoxic

Has tendency to penetrate and cause **invasive colitis**

Other Toxins

- Cytoskeletal disruption –

causes **loss of tight junctions** in intestinal epithelium

Eg: **Bft toxin** of ***Bacteroides fragilis***

disrupts tight junctions, leading to an inflammatory diarrhea

C. difficile toxin - disrupt epithelial integrity

Antibiotic-Associated Colitis

TABLE 96-1 Antimicrobial and Chemotherapeutic Agents Associated with *Clostridium difficile* Diarrhea or Colitis

More Frequently Associated Agents	*Less Frequently Associated Agents*
Cephalosporins (especially second- and third-generation agents)	Ticarcillin-clavulanate
Ampicillin and amoxicillin	Chloramphenicol
Clindamycin	Metronidazole
Fluoroquinolones	Amphotericin B
Other penicillins, including β-lactamase–stable penicillins	Rifampin
Erythromycin and other macrolides	5-Fluorouracil
Tetracyclines	Methotrexate
Trimethoprim-sulfamethoxazole	Doxorubicin
	Cyclophosphamide
	Aminoglycosides
	Sulfonamides

Diagnosis
C. difficile–associated disease

TABLE 96-2 Sensitivity and Specificity of Tests for the Diagnosis of *Clostridium difficile*–Associated Disease

Test	*Sensitivity (%)**	*Specificity (%)**	*Utility of Test*
Endoscopy	51	~100	Diagnostic of PMC
Culture for *C. difficile*	89-100	84-99	Highly sensitive; confirmation of organism toxicity optimal
Cell culture cytotoxin test	67-100	85-100	With clinical data, diagnostic of CDAD
EIA toxin test	63-99	75-100	With clinical data, diagnostic of CDAD
Latex test for *C. difficile* antigen	58-92	80-96	Less sensitive and specific than other tests; rapid results
PCR toxin gene detection	Undetermined	Undetermined	Research test

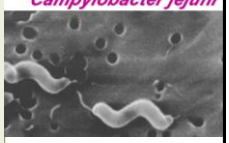
Other Toxins

- *V. cholerae* - **zonula occludens toxin**
  causes paracellular leak
  contribute to the diarrhea of cholera
- EAEC - The **plasmid-encoded cytotoxin** (Pet)
  Causes - fluid secretion and
  - ultra structural changes in the intestinal epithelium

Campylobacter

- *Campylobacter jejuni subsp. Jejuni* is the most important spp (89–93%)
- Produce **mild** short-term diarrhoea of 2 days to a **severe** form
- The diarrhoea is watery and **may contain blood**.
- Vomiting – occasional
- The diarrhoea may be accompanied by severe pain

Campylobacter jejuni



Enteric Fever and Other Causes of Abdominal Symptoms with Fever

- Characterized by abdominal pain and fever.
- After a systemic phase, these infections subsequently involve intestinal tissue & manifest as
  - Enteric fever
  - Mesenteric adenitis
    - a syndrome that may mimic **acute appendicitis**, caused by several bacteria

Enteric fever

TABLE 98-2 Frequency of Symptoms and Physical Findings in Patients with Enteric Fever

Parameter	*Typhoid Fever (%)**	*Paratyphoid A and B (%)†*
Symptoms		
Fever	39-100	92-100
Headache	43-90	60-100
Nausea	23-36	33-58
Vomiting	24-35	22-45
Abdominal cramps	8-52	29-92
Diarrhea	30-57	17-68
Constipation	10-79	2-29
Cough	11-86	10-68
Physical findings		
Fever	98-100	100
Abdominal tenderness	33-84	6-29
Splenomegaly	23-65	0-74
Hepatomegaly	15-52	16-32
Relative bradycardia	17-50	11-100
Rose spots	2-46	0-3
Rales or rhonchi	4-84	2-87
Epistaxis	1-21	2-13
Meningismus	1-12	0-3

Whipple's Disease

- Rare **systemic** infectious disorder caused by *Tropheryma whipplei*.
- Chronic disease
- Present with **weight loss, arthralgia, diarrhea, & abdominal pain**
- Ass/w various other clinical patterns (involvement of the heart, lung, or (CNS), are frequent.
- The diagnosis is via **small bowel biopsy**

Specific antimicrobial therapy for infectious diarrhea

- Indicated in a limited number of situations

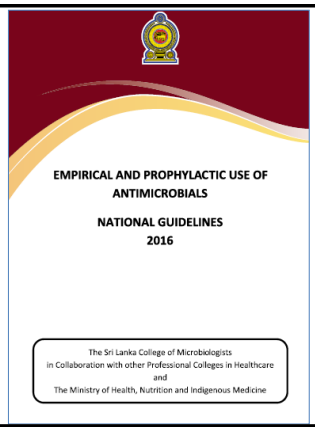
  Eg: Acute traveler's diarrhea

  Shigellosis

  Campylobacteriosis

  Typhoid fever

  Bacteremic salmonellosis



Approach to diagnosis and management of infectious diarrhoea.