# GASTROINTESTINAL TRACT INFECTIONS

Chapter 12

## HELICOBACTER PYLORI

*Helicobacter pylori* is a bacterium that is found in the gastric mucous layer or adherent to the epithelial lining of the stomach. It is a common cause of gastric and duodenal ulcers. Its route of transmission remains unknown but current data suggests a faecal-oral route. The organism's urease enzyme, motility and ability to adhere to gastric epithelium are factors that enable the organism to survive and proliferate in the gastric milieu. Recent adult European guidelines (Maastricht 2016) describe *H. pylori* as a cause of chronic active gastritis in all colonised adult patients.

### DIAGNOSIS

Diagnostic tests involve invasive or non-invasive techniques. The choice is based upon the need for endoscopy, cost, availability, clinical situation and population prevalence of the infection. Bedside testing may be performed using the urea breath test.

Diagnostic tests include:

| NON-INVASIVE | INVASIVE (BIOPSY) |
|---|---|
| • Stool: *H. pylori* antigen (rapid test) | • Histological examination |
| • Blood: *H. pylori* IgG | • Bacterial culture and sensitivity |
| • Urease breath test | • Polymerase chain reaction (PCR) |

### TREATMENT

According to the European Helicobacter study group, *H. pylori* infection in an adult should be treated regardless of a patient's symptoms or stage of disease. This includes:

- Patients with active peptic ulcer disease
- Patients with a past documented history of a peptic ulcer
- Patients that had undergone resection for early stage gastric cancer and in patients with gastric MALT lymphomas
- Asymptomatic patients with a positive *H. pylori* test

The optimal treatment regimen has not yet been defined. Triple therapy for 14 days, consisting of two antibiotics and a proton pump inhibitor is advised for initial empiric treatment. Resistance to amoxicillin remains low; however, studies show variable primary resistance to clarithromycin depending on the geographical region. There is also an increasing prevalence of secondary resistance to clarithromycin and metronidazole. Treatment failures are frequent when short course therapy is used and with infections due to resistant strains of *H. pylori*. Quadruple therapy is an alternative initial regimen in areas with a high prevalence of resistance (> 15%) to clarithromycin and metronidazole, or with recent or repeated exposure to clarithromycin and metronidazole. For

patients that fail initial triple therapy, a second-line regimen with bismuth-containing quadruple therapy is advised. Eradication of *H. pylori* must be confirmed by means of follow-up testing from four weeks after completion of therapy. Treatment failure occurs due to either patient non-compliance or antibiotic resistance.

**TRIPLE THERAPY (INITIAL REGIMEN, NO PAST CLARITHROMYCIN EXPOSURE)**

Proton Pump Inhibitor (PPI) PO 12 hourly
**AND**
Amoxicillin 1 g PO 12 hourly OR metronidazole 400 mg PO 12 hourly
**AND**
Clarithromycin 500 mg PO 12 hourly
Treat for 14 days

**NON-BISMUTH QUADRUPLE THERAPY (ALTERNATIVE INITIAL REGIMEN)**

Proton Pump Inhibitor (PPI) PO 12 hourly
**AND**
Amoxicillin 1 g PO 12 hourly
**AND**
Metronidazole 400 mg PO 12 hourly
**AND**
Clarithromycin 500 mg PO 12 hourly
Treat for 14 days
Note: If penicillin allergic, use bismuth quadruple therapy

**BISMUTH QUADRUPLE THERAPY (ALTERNATIVE INITIAL REGIMEN, SECOND-LINE REGIMEN FOR FAILED TRIPLE THERAPY)**

Proton Pump Inhibitor (PPI) PO 12 hourly
**AND**
Bismuth 240 mg PO 12 hourly
**AND**
Tetracycline 500 mg PO 12 hourly OR doxycycline 100 mg PO 12 hourly
**AND**
Metronidazole 400 mg PO 12 hourly
Treat for 14 days

Patients that fail a second-line regimen should have samples sent for culture and susceptibility testing. A fluoroquinolone containing triple or quadruple regimen is recommended. In cases of suspected fluoroquinolone resistance, combination with bismuth and rifabutin may be an option.

**FLUOROQUINOLONE TRIPLE THERAPY (FOR FAILED SECOND-LINE THERAPY)**

Proton Pump Inhibitor (PPI) PO 12 hourly

**AND**

Amoxicillin 1 g PO 12 hourly OR metronidazole 400 mg PO 12 hourly (penicillin-allergic individuals)

**AND**

Levofloxacin 500 mg PO 12 hourly

Treat for 14 days

**NOTE**

Meta-analyses have shown better results with a levofloxacin-containing regimen than with the quadruple combination for second-line therapy and with fewer side effects. Conversely, there has been an increase in primary fluoroquinolone resistance and this may affect levofloxacin-based regimens. Levofloxacin should not be used for first-line regimens due to increasing resistance to this antibiotic.

**PROTON PUMP INHIBITOR OPTIONS – USE ONE OF THE FOLLOWING:**

Lansoprazole 30 mg PO 12 hourly

Omeprazole 20 mg PO 12 hourly

Pantoprazole 40 mg PO 12 hourly

Rabeprazole 20 mg PO 12 hourly

Esomeprazole 20 mg PO 12 hourly

# BACTERIAL CAUSES OF INFECTIOUS DIARRHOEA

## CLOSTRIDIUM DIFFICILE ANTIBIOTIC-ASSOCIATED DIARRHOEA (CDAD)

*Clostridium difficile* infection (CDI) is one of the most common hospital-acquired infections and causes antibiotic-associated pseudomembranous colitis (CDAD). It is acquired through colonisation of the intestinal tract via the faecal-oral route, facilitated by disruption of normal intestinal flora due to antimicrobial therapy. Patients with *C. difficile* carriage are a reservoir for environmental contamination in the presence or absence of clinical infection. *C. difficile* is highly transmissible via the faecal-oral route by ingestion of spores.

### PATHOGENESIS

- *C. difficile* elaborates two potent exotoxins (toxin A and B) that cause colitis and diarrhoea.
- Toxin A is an enterotoxin which causes inflammation leading to intestinal fluid secretion and mucosal injury.
- Toxin B is a cytotoxin which causes colonic mucosal damage.
- The toxins bind to receptors on intestinal epithelial cells, leading to inflammation and diarrhoea.
- The hypervirulent strain (NAP1/BI/027) produces an additional toxin, the binary toxin.

### RISK FACTORS

- Antibiotics: fluoroquinolones, clindamycin, broad-spectrum penicillins and cephalosporins
- Gastric acid suppression: proton pump inhibitors, histamine-2 receptor antagonists
- Cancer chemotherapy due to their antimicrobial effect on the gastrointestinal tract
- Gastrointestinal surgery and haematopoietic stem cell transplantation

**CLINICAL**

- The spectrum of disease ranges from asymptomatic carriage to colitis to fulminant colitis and toxic megacolon.
- Cardinal symptoms are watery diarrhoea with lower abdominal pain and fever.
- Leukocytosis (WBC >15 000/μL) is usually a common finding.

**DIAGNOSIS**

Laboratory testing should be requested only for patients with diarrhoea and a clinically compatible illness. PCR testing for the toxin genes is performed as the first-line test for *C. difficile* at Ampath. PCR is a very sensitive test that can be performed quickly allowing for a rapid diagnosis and thus the timeous implementation of appropriate antimicrobial therapy and infection control procedures.

**TREATMENT**

- Treatment is indicated in patients who are symptomatic and have a positive diagnostic test.
- Treatment is not indicated in asymptomatic patients with positive laboratory results.
- Empiric therapy can be administered pending the results of diagnostic testing if clinical suspicion is high.
- The initial step in the treatment of CDAD is cessation of the inciting antibiotic.
- If ongoing antibiotics are essential for treatment of the primary infection, select antibiotic therapy that is less frequently implicated in antibiotic-associated CDI.
- Implement appropriate infection control procedures which include contact precautions and hand washing with soap and water.
- For relapsing infections please consult a microbiologist for treatment advice.

**C. DIFFICILE TREATMENT: MILD TO MODERATE DISEASE**

| ADULTS | TREATMENT DURATION |
|---|---|
| Metronidazole 400 mg PO 8 hourly | Treat for 10–14 days |
| **CHILDREN** | **TREATMENT DURATION** |
| Metronidazole 7.5 mg/kg PO 8 hourly<br>OR<br>Metronidazole 30 mg/kg PO 6 hourly | Treat for 10–14 days |

**C. DIFFICILE TREATMENT: SEVERE DISEASE**

| ADULTS | TREATMENT DURATION |
|---|---|
| Vancomycin 125 mg PO 6 hourly<br>If no clinical improvement increase dose of vancomycin to 500 mg PO 6 hourly | Treat for 10–14 days |
| **CHILDREN** | **TREATMENT DURATION** |
| Vancomycin 40 mg/kg/day PO in 4 divided doses | Treat for 10–14 days |

**NOTE:** IV vancomycin is not excreted into the colon and must be given PO

**C. DIFFICILE TREATMENT: CRITICALLY ILL WITH FULMINANT OR REFRACTORY DISEASE**

| ADULTS | TREATMENT DURATION |
|---|---|
| Vancomycin 500 mg PO 6 hourly<br>**AND**<br>Metronidazole 500 mg IV 6 hourly | Treat for 10–14 days |

In a retrospective study of ICU patients vancomycin and metronidazole combination was associated with a significant decrease in mortality (CID 61:934, 2015)

**C. DIFFICILE TREATMENT: SALVAGE THERAPY**

| ADULTS | TREATMENT DURATION |
|---|---|
| Tigecycline 100 mg IV loading dose FOLLOWED BY 50 mg IV 12 hourly | Treat for 10–14 days |

**C. DIFFICILE TREATMENT: TREATMENT FAILURE AND RELAPSE**

| ADULTS | TREATMENT DURATION |
|---|---|
| First relapse: repeat course of vancomycin 125 mg PO 6 hourly<br>Second relapse: vancomycin tapered treatment 125 mg PO 6 hourly for 14 days, FOLLOWED BY 125 mg PO 8 hourly for 7 days, FOLLOWED BY 125 mg PO 12 hourly for 7 days, FOLLOWED BY 125 mg PO once daily for 7 days, FOLLOWED BY 125 mg PO every 48 hours for 7 days, FOLLOWED by 125 mg PO every 72 hours for 7 days<br>**Other therapies:**<br>Faecal microbiota transplant used in place of vancomycin taper treatment<br>Fidaxomicin (not yet available in South Africa) | Treat for 10–14 days (first relapse) |

## SALMONELLA INFECTION

There are many types of *Salmonella* and they can be divided into two broad categories: those that cause typhoid and enteric fever and those that primarily result in gastroenteritis. *Salmonella enteritidis* and *Salmonella typhimurium* are non-typhoidal *Salmonella* (NTS) and the most frequently isolated serotypes of *Salmonella* causing gastroenteritis. Classic typhoid or enteric fever is caused by *S. typhi* and *S. paratyphi*. NTS are commonly implicated in food-borne infections and outbreaks and are associated with animal reservoirs, especially poultry and eggs. This can result in acute self-limited gastroenteritis. Typhoid is a systemic illness characterised by fever, abdominal pain and bacteraemia.

### CLINICAL

- NTS infection: symptoms occur within eight to 72 hours of ingesting contaminated food or water and include nausea, vomiting, diarrhoea and cramping. Diarrhoea is self-limiting and usually resolves within four to ten days.
- Typhoid fever is typically described having characteristic stages of the infection. Early infection features a rising temperature, relative bradycardia followed by abdominal pain and “rose spots” in the second week. During the third week of the illness, hepatosplenomegaly, intestinal bleeding and possible perforation of infected Peyer’s patches in the colon are features.

- Invasive disease is characterised by bacteraemia and extra-intestinal manifestations which include endocarditis, mycotic aneurysms and osteomyelitis.
- NTS is a leading cause of community-acquired bacteraemia in HIV-infected adults, especially in sub-Saharan Africa. In immune-competent adults, invasive disease occurs in less than 5% of cases, especially at the extremes of age.

**DIAGNOSIS**

- Gastroenteritis: Stool microscopy and culture
- Invasive disease: Blood culture, stool culture, bone marrow culture (complicated cases or when diagnosis uncertain)
- Stool PCR: Ampath offers a bacterial gastroenteritis multiplex PCR which tests for *Salmonella* spp., *Shigella* spp., *Campylobacter* spp. (jejuni and coli), enteroinvasive *E. coli* (EIEC) and Shiga toxins (stx1 and stx2) found in Shiga toxin-producing *E. coli* (STEC) and *Shigella dysenteriae*

**TREATMENT**

- Fluid and electrolyte replacement is the cornerstone of therapy
- Antibiotic therapy should be considered in the following patients:
  - Infants and children up to two years of age
  - Adults over 50 years of age
  - Immunocompromised patients: organ transplant patients, HIV-infected patients, patients with cancer and lymphoproliferative disease, sickle cell disease
  - Patients with vascular grafts or prosthetic joints
  - Patients with severe disease (high fever, more than nine or 10 stools per day)
- The antibiotic choice should be made according to the local antibiotic susceptibility pattern as the prevalence of antibiotic resistance to NTS is increasing worldwide.

| Rx | **NON-TYPHOIDAL SALMONELLA (NTS) INFECTION (INTESTINAL)** | **USUALLY SELF-LIMITING AND ROUTINE ANTIBIOTICS ARE NOT RECOMMENDED** |
|---|---|---|
| | **ORAL THERAPY IN HIGH RISK PATIENTS** | |
| | **ADULTS** | **TREATMENT DURATION** |
| | Ciprofloxacin 400 mg PO 12 hourly<br>OR<br>Levofloxacin 500 mg PO once daily<br>OR<br>Azithromycin 500 mg PO once daily | Treat for 7–14 days |
| | **CHILDREN** | **TREATMENT DURATION** |
| | Azithromycin (> 28 months of age) 5–12 mg/kg PO once daily<br>OR<br>Cotrimoxazole 8–12 mg/kg daily divided and given 12 hourly | Treat for 7–14 days |

**NON-TYPHOIDAL SALMONELLA (NTS) INFECTION (EXTRA-INTESTINAL/INVASIVE DISEASE)**

**ANTIBIOTIC**

| ADULTS | TREATMENT DURATION |
|---|---|
| Ciprofloxacin 400 mg IV 12 hourly OR levofloxacin 750 mg IV once daily<br>OR<br>Ceftriaxone 2 g IV once daily<br>OR<br>Cefotaxime 2 g IV 8 hourly | Usually 14 days but duration is based on the site of infection |
| **CHILDREN** | **TREATMENT DURATION** |
| Ceftriaxone 50 mg/kg IV once daily | Usually 14 days but duration is based on the site of infection |

**TYPHOID FEVER**

**ANTIBIOTIC**

| ADULTS | TREATMENT DURATION |
|---|---|
| Ciprofloxacin 400 mg IV 12 hourly OR levofloxacin 750 mg IV once daily<br>OR<br>Ceftriaxone 2 g IV once daily<br>Do not use a quinolone for infections acquired in Asia due to high rates of resistance<br>For severely ill patients add dexamethasone 3 mg/kg IV just before the first dose of antibiotic, followed by 1 mg/kg 6 hourly x 8 doses | Treat for 7–10 days |
| **CHILDREN** | **TREATMENT DURATION** |
| Ceftriaxone 50 mg/kg IV once daily | Treat for 14 days |

### CHRONIC CARRIAGE

Chronic carriage is defined as the shedding of *Salmonella* in stool for more than one year, as documented by an initial positive culture obtained at least one month after resolution of the acute illness and repeat positive cultures. Chronic carriers do not develop clinical disease and while they excrete large amount of organisms they have a robust immune response to *Salmonella*. Treatment of persons with asymptomatic carriage of NTS is controversial. Optimal treatment for chronic carriage is not well studied but includes fluoroquinolone treatment for four to six weeks.

## SHIGELLA INFECTION

Bacillary dysentery due to *Shigella* species is a major cause of morbidity and mortality. Shigellosis has a worldwide incidence of about 165 million cases annually and one million associated deaths. Transmission typically occurs though contaminated food and water with shigellosis being the most transmissible of the bacterial diarrhoeas. There are four different species of *Shigella*; *Shigella sonnei*, *Shigella flexneri, Shigella boydii* and *Shigella dysenteriae.*

**CLINICAL**

- Symptoms include high fever, abdominal cramps and dysentery (small volume, bloody and mucoid stools)
- *Shigella* gastroenteritis is generally self-limiting

**DIAGNOSIS**

- Stool culture
- Stool PCR: Ampath offers a bacterial gastroenteritis multiplex PCR which tests for *Salmonella* spp., *Shigella* spp., *Campylobacter* spp. (*jejuni* and *coli*), Enteroinvasive *E. coli* (EIEC) and Shiga toxins (stx1 and stx2) found in Shiga toxin-producing *E. coli* [STEC] and *Shigella dysenteriae.*

**TREATMENT**

- Fluid and electrolyte replacement is important
- Intestinal anti-motility drugs such as loperamide should be avoided
- Antibiotics have been shown to decrease the duration of fever and diarrhoea by about two days and therefore shorten the duration of shedding and possibly reduce person-to-person spread.
- Antibiotics are recommended for:
  - Severely ill patients with diarrhoea requiring hospitalisation
  - Elderly patients
  - Malnourished patients
  - Food handlers, healthcare workers and individuals in day-care centres (children and caregivers)
- In children under 18 years, intravenous antibiotic therapy is indicated if:
  - There is underlying immune deficiency
  - There is severe toxaemia and bacteraemia
  - Patients are unable to take oral medication

The choice of antibiotics is dependent on the local resistance pattern of *Shigella* spp.

**SHIGELLOSIS: EMPIRIC ANTIBIOTICS**

**ORAL THERAPY**

| **ADULTS** | **TREATMENT DURATION** |
|---|---|
| Ciprofloxacin 500 mg PO 12 hourly<br>OR<br>Ciprofloxacin 750 mg PO once daily<br>OR<br>Levofloxacin 500 mg PO once daily<br>OR<br>Azithromycin 500 mg PO once daily | Immunocompetent/not *S. dysenteriae*: 3 days<br>*S. dysenteriae*: 5–7 days<br>Immunocompromised: 7–10 days |
| **CHILDREN** | **TREATMENT DURATION** |
| Azithromycin 10 mg/kg PO once daily (first-line choice) | Immunocompetent/not *S. dysenteriae*: 3 days<br>*S. dysenteriae*: 5–7 days<br>Immunocompromised: 7–10 days |

| Rx | INTRAVENOUS THERAPY | |
|---|---|---|
| | **ADULTS** | **TREATMENT DURATION** |
| | Ceftriaxone 1–2 g IV once daily | Treat for 5 days |
| | **CHILDREN** | **TREATMENT DURATION** |
| | Ceftriaxone 50 mg/kg/day IV once daily | Treat for 5 days |

## CAMPYLOBACTER INFECTION

*Campylobacter* infection is an important cause of acute diarrhoea worldwide. Infections may also produce a systemic illness. *Campylobacter* enteritis is typically caused by *Campylobacter jejuni* or *Campylobacter coli*. *C. jejuni* is a commensal of the gastrointestinal tract of a wide range of animal hosts such as poultry, cattle and sheep. Common sources of infection include consumption of undercooked meat and unpasteurised milk. Other sources of infection include occupational exposure of farmers and laboratory workers and through contaminated food.

### CLINICAL

- Campylobacter infections are self-limiting
- Acute illness is characterised by peri-umbilical abdominal cramps and diarrhoea (may be bloody)
- Acute onset complications: cholecystitis, peritonitis, pericarditis and myocarditis
- Late onset complications: reactive arthritis and Guillian-Barré syndrome
- Symptoms and signs mimicking pseudo-appendicitis and colitis may also occur

### DIAGNOSIS

- Stool: culture
- Stool PCR: Ampath offers a bacterial gastroenteritis multiplex PCR which tests for *Salmonella* spp., *Shigella* spp., *Campylobacter* spp. *(jejuni* and *coli*), Enteroinvasive *E. coli* (EIEC) and Shiga toxins (stx1 and stx2) found in Shiga toxin-producing *E. coli* [STEC] and *Shigella dysenteriae.*

### TREATMENT

- Fluid and electrolyte replacement should be the focus of therapy
- Antibiotics are not necessary for most cases of *Campylobacter* gastroenteritis
- Antibiotics are recommended for severe disease:
  - Bloody stools
  - High fever
  - Extra-intestinal infection
  - Symptoms over a week or worsening symptoms
  - Those at risk of severe disease (elderly, pregnant, immunocompromised)
- Intravenous antibiotic therapy is indicated in:
  - Severely ill patients
  - Patients who cannot tolerate oral treatment

| CAMPYLOBACTER: EMPIRIC ANTIBIOTICS | |
|---|---|
| **ORAL THERAPY** | |
| **ADULTS** | **TREATMENT DURATION** |
| Azithromycin 500 mg PO once daily<br>OR<br>Ciprofloxacin 750 mg PO 12 hourly<br>OR<br>Levofloxacin 500 mg PO once daily | Usually 3 days<br>Immunocompromised: 7–14 days<br>With complications: 7–14 days |
| **CHILDREN** | **TREATMENT DURATION** |
| Azithromycin 10 mg/kg PO once daily | Usually 3 days<br>Immunocompromised: 7–14 days<br>With complications: 7–14 days |
| **INTRAVENOUS THERAPY** | **TREATMENT DURATION** |
| A carbapenem or fluoroquinolone | Duration is based on the site of infection and response to therapy |

## ESCHERICHIA COLI INFECTION

*Escherichia coli* are normal inhabitants of the human gastrointestinal tract, however strains can acquire certain genetic material and become pathogenic. *E. coli* are among the most frequent bacterial causes of diarrhoea and are classified by the clinical syndrome they produce. Transmission is typically through contaminated food and water.

### CLINICAL

The clinical syndromes produced by the various pathogenic *E. coli* can be seen in the table below. Pathogenic *E. coli* have certain virulence factors such as toxin production that result in the clinical manifestations observed.

| STRAIN | SYNDROME |
|---|---|
| Enterotoxigenic *E. coli* (ETEC) | Watery diarrhoea. A common cause of travellers' diarrhoea |
| Enteropathogenic *E. coli* (EPEC) | Acute diarrhoea in infants and children |
| Enterohaemorrhagic *E. coli* (EHEC) | Haemorrhagic colitis and haemolytic uremic syndrome (HUS). Also referred to as Shiga toxin-producing E. coli (STEC) |
| Enteroinvasive *E. coli* (EIEC) | Dysentery. Causes a disease very similar to shigellosis |
| Enteroaggregative *E. coli* (EAEC) | Persistent diarrhoea in children and patients with HIV |

Wanke CA. Pathogenic *Escherichia coli* in: *UpToDate*, edited by SB Calderwood, Waltham MA. (Accessed on June 27, 2016.)

**DIAGNOSIS**

- *E. coli* can easily be cultured from stool specimens in the laboratory. Pathogenic *E. coli* cannot be differentiated from each other based on the culture appearance or biochemical tests and additional laboratory tools such as PCR need to be used to identify the presence of a pathogenic strain.
- Stool PCR: Ampath offers a bacterial gastroenteritis multiplex PCR which tests for *Salmonella* spp., *Shigella* spp., *Campylobacter* spp. *(jejuni* and *coli*), Enteroinvasive *E. coli* (EIEC) and Shiga toxins (stx1 and stx2) found in Shiga toxin-producing *E. coli* [STEC/EHEC] and *Shigella dysenteriae.*

**TREATMENT**

Regardless of the pathogenic strain, all cases of *E. coli* diarrhoea require attention to hydration with appropriate fluid management and observing for potential complications. Generally, antimotility agents should be avoided as they are not beneficial, may increase risks of complications and mask the amount of fluid loss in the intestine.

The role of antibiotics depends on the pathogenic strain, if identified by the laboratory. Empiric therapy with either ciprofloxacin or levofloxacin for three to five days is indicated with severe diarrhoea with blood and/or mucous in the stool.

**ETEC:** Antibiotics can shorten the duration of travellers' diarrhoea, however, are not usually necessary unless there is severe diarrhoea or blood and/or mucous in the stool.

**ETEC/TRAVELLERS' DIARRHOEA: EMPIRIC ANTIBIOTICS**

**ORAL THERAPY**

| **ADULTS** | **TREATMENT DURATION** |
|---|---|
| Ciprofloxacin 500 mg PO 12 hourly<br>OR<br>Azithromycin 1 g PO as a single dose | 3 days (ciprofloxacin) |
| **CHILDREN** | **TREATMENT DURATION** |
| Ciprofloxacin 20–30 mg/kg/day PO given 12 hourly<br>OR<br>Azithromycin 10 mg/kg PO as a single dose | 3 days (ciprofloxacin) |

**EPEC/watery diarrhoea in children:** Antibiotics are not indicated

**EHEC:** Antibiotics are generally not indicated as they have not been found to be beneficial and may increase the risk of developing HUS.

**EIEC:** Antibiotics should be given as for *Shigella* infections

**EAEC:** Quinolone antibiotics have been shown to reduce the duration of diarrhoea

**EAEC: EMPIRIC ANTIBIOTICS**

**ORAL THERAPY**

| **ADULTS** | **TREATMENT DURATION** |
|---|---|
| Ciprofloxacin 500 mg PO 12 hourly | 3 days |
| **CHILDREN** | **TREATMENT DURATION** |
| Ciprofloxacin 20–30 mg/kg/day PO given 12 hourly | 3 days |

## CHOLERA INFECTION

Cholera is an acute, diarrhoeal illness caused by infection of the intestine by the bacterium *Vibrio cholerae*. Globally, it is reported to cause three to five million cases with ~100 000 deaths annually.

### CLINICAL

- The infection is often mild or without symptoms
- Approximately 1:10 infected persons will develop a severe infection characterised by severe watery diarrhoea with flecks of mucus, 'rice-water' stools and vomiting.
- Massive volume and electrolyte losses can lead to dehydration and shock

### DIAGNOSIS

Stool: microscopy and culture

### TREATMENT

- The mainstay of therapy is fluid and electrolyte replacement given orally or intravenously as required.
- Antibiotics serve as an adjunct to appropriate rehydration. Antibiotics have two beneficial effects:
  - Reduce the duration of diarrhoea by approximately 50%
  - Reduce the duration of organism shedding to around one to two days

**CHOLERA: EMPIRIC ANTIBIOTIC**

**ORAL THERAPY**

| ADULTS | TREATMENT DURATION |
|---|---|
| Doxycycline 300 mg PO as a single dose<br>OR<br>Tetracycline 500 mg PO 6 hourly<br>OR<br>Azithromycin 1 g PO as a single dose | 3 days (tetracycline) |
| **CHILDREN** | |
| Azithromycin 20 mg/kg PO as a single dose<br>Antibiotics are given orally once the vomiting stops | |

## YERSINIA INFECTION

Yersiniosis is caused by *Y. enterocolitica* and *Y. pseudotuberculosis*. *Y. enterocolitica* is most commonly implicated. Yersiniosis is a zoonotic infection of domestic and wild animals. Humans are considered incidental hosts.

### CLINICAL

- Clinical manifestations include acute yersiniosis and pseudoappendicitis syndrome due to mesenteric adenitis.
- Acute yersiniosis features include diarrhoea, abdominal pain, fever, nausea and vomiting.
- Localisation of abdominal pain to the right lower quadrant may be a diagnostic clue for yersiniosis.

- Pharyngitis may occur in up to 20% of cases and can be a helpful diagnostic clue since no other cause of acute bacterial diarrhoea causes pharyngitis.
- Pseudoappendicitis occurs when acute yersiniosis presents with right lower abdominal pain, fever, vomiting, leukocytosis and understated diarrhoea, thus mimicking acute appendicitis.
- A number of extra-intestinal complications can also occur due to infection outside of the gastrointestinal tract.

**DIAGNOSIS**

- Microbiological culture of stool, mesenteric lymph nodes, pharyngeal exudates, peritoneal fluid and blood.
- Serology with a positive IgM as well as a fourfold rise in IgG antibody titres between acute and convalescent specimens, supporting a diagnosis of acute yersiniosis.

**TREATMENT**

Antimicrobial therapy for acute, uncomplicated yersiniosis has not been proven to be beneficial. Antimicrobial treatment is only recommended for severe disease.

**YERSINIA: EMPIRIC ANTIBIOTICS**

| ORAL THERAPY | |
|---|---|
| **ADULTS**<br>Ciprofloxacin 500 mg PO 12 hourly | **TREATMENT DURATION**<br>5 days |
| **CHILDREN**<br>Cotrimoxazole TMP 8 mg/kg/day and SMX 40 mg/kg/day PO in two divided doses | **TREATMENT DURATION**<br>5 days |
| **INTRAVENOUS THERAPY** | |
| **ADULTS**<br>Ceftriaxone 2 g IV given once daily<br>**AND**<br>Gentamicin 5 mg/kg/day IV given once daily | **TREATMENT DURATION**<br>Extra-intestinal infections and septicaemia should be treated for 3 weeks (switch to oral treatment once clinically improved) |
| **CHILDREN**<br>Ceftriaxone 100 mg/kg/day IV in two divided doses<br>**AND**<br>Gentamicin 5 mg/kg/day IV given once daily | **TREATMENT DURATION**<br>Extra-intestinal infections and septicaemia should be treated for 3 weeks (switch to oral treatment once clinically improved) |

## VIRAL CAUSES OF INFECTIOUS DIARRHOEA

Acute viral gastroenteritis is a common cause of diarrhoea and vomiting in both adults and children. Transmission of viral pathogens occurs via the faecal-oral route. In addition, viruses can cause outbreaks in closed communities such as nursing homes, schools and cruise ships. Contaminated food in restaurants and catered food can also result in outbreaks. The following viruses cause acute viral gastroenteritis:

- **Rotavirus:** typically in children between six months and two years of age with autumn/winter predominance. Incidence is falling with the immunisation of infants.

- **Norovirus:** occurs in people of all ages, highly contagious and a common cause of food- or water-borne outbreaks.
- **Sapovirus:** typically affects infants and toddlers and causes a milder illness than rotavirus.
- **Astrovirus:** occurs in persons of all age but primarily in children under five years.
- **Enteric adenovirus (adenovirus 40/41):** typically affects children under five years.

#### CLINICAL

- The incubation period varies from about 12 to 60 hours and the symptoms typically last for three to seven days.
- Clinical presentation is similar with gastroenteritis caused by viruses and bacterial pathogens, however the presence of blood and mucous should prompt investigation and treatment of a bacterial pathogen.
- The most common reported symptoms are nausea, diarrhoea, vomiting (esp. with norovirus infections), fever and abdominal pain.

#### DIAGNOSIS

- The diagnosis can be suggested by the history of rapid onset of diarrhoea of short duration accompanied by nausea, vomiting, abdominal pain and fever.
- Rapid antigen tests can be performed on stool for rotavirus and enteric adenoviruses.
- Stool microscopy and culture can be used to detect a bacterial or parasitic cause when suspected.
- Stool PCR: Ampath offers a viral gastroenteritis multiplex PCR which detects rotavirus, norovirus genogroup one and two, adenovirus, astrovirus and sapovirus. This is considered the gold standard test for viral gastroenteritis.

#### TREATMENT

- No specific pharmacologic therapy is required and the disease is self-limiting.
- Treatment is largely supportive with a focus on fluid repletion and treating dehydration if present.
- Antibiotics should not be given unless a bacterial cause that warrants antibiotics is identified as the cause.
- Anti-diarrheal (e.g. kaolin-pectin) and antimotility agents (e.g. loperamide) are contraindicated in the treatment of acute gastroenteritis in children because of their lack of benefit and increased risk of side effects, including ileus, drowsiness and nausea.
- Antimotility and antiemetics can be used in adult patients.
- Probiotics may be effective in reducing the duration of diarrhoea.

## PARASITIC CAUSES OF INFECTIOUS DIARRHOEA

### AMOEBIASIS

Intestinal amoebiasis is caused by the protozoan *Entamoeba histolytica.* Globally, *Entamoeba histolytica* accounts for 40 to 50 million cases of colitis or extra-intestinal disease annually. About 40 000 deaths occur worldwide. The parasite exists in two forms; cysts (infectious) and trophozoites (cause invasive disease). Transmission is by means of ingestion of amoebic cysts via contaminated food and water.

## CLINICAL

- About 90% of *E. histolytica* infections are asymptomatic. Diarrhoea is the most common clinical manifestation.
- Symptoms range from mild diarrhoea to severe dysentery and fulminant amoebic colitis.
- Complications include extra-intestinal infections, amoebic liver abscess (ALA), pulmonary, brain and cardiac involvement.

## DIAGNOSIS

Diagnosis is traditionally accomplished by the combination of serology or stool antigen testing with identification of parasites in stool or aspirates from liver abscesses by microscopy. Recently PCR testing on stool has become the preferred test due to better sensitivity and specificity compared to existing tests.

- **Stool microscopy:** demonstration of cysts or trophozoites suggests intestinal amoebiasis. A minimum of three specimens on separate days detects 85 to 95% of infections.
- **Serology:** antibodies are detectable within five to seven days of acute infection. Negative serology is helpful for exclusion of disease. Positive serology cannot distinguish acute from previous infection and must be combined with stool microscopy.
- **Antigen testing:** sensitive, specific and rapid. Uses monoclonal antibodies to detect *E. histolytica* derived Gal/GalNAC lectin in stool.
- **PCR:** Ampath offers a multiplex stool parasite PCR which detects *Entamoeba histolytica, Giardia lamblia* and *Cryptosporidium* species.

## TREATMENT

Antimicrobial therapy for *E. histolytica* infection is always advised, even in asymptomatic cases, due to the potential risk of developing invasive disease and spread to family members. The goal of antimicrobial therapy is to eliminate the invading trophozoites and to eradicate intestinal carriage of the organism.

**E. HISTOLYTICA: EMPIRIC ANTIMICROBIALS**

**MILD/MODERATE DISEASE**

**ADULTS**

Metronidazole 400–800 mg PO 8 hourly for 7–10 days

OR

Tinidazole 2 g PO once daily for 3 days

**CHILDREN**

Metronidazole 35–50 mg/kg/day PO given 8 hourly for 7–10 days

OR

Tinidazole 60 mg/kg PO once daily for 3 days

**SEVERE DISEASE**

Metronidazole 750 mg IV 8 hourly for 10 days (switch to oral metronidazole once clinically improving)

OR

Tinidazole 2 g PO once daily for 5 days

**TO ERADICATE INTESTINAL CYSTS THE FOLLOWING TREATMENT SHOULD FOLLOW THE INITIAL TREATMENT**

**ADULTS**

Paromomycin 25–30 mg/kg per day PO given 8 hourly for 7 days

OR

Diiodohydroxyquin 650 mg PO given 8 hourly for 20 days

OR

Diloxanide furoate 500 mg PO given 8 hourly for 10 days

**CHILDREN**

Diiodohydroxyquin 30–40 mg/kg per day PO given 8 hourly for 20 days

OR

Diloxanide furoate 20 mg/kg per day PO given 8 hourly for 10 days

## GIARDIASIS

*G. lamblia* (also known as *G. duodenalis* or *G. intestinalis*) is a flagellated protozoan parasite and causes epidemic and sporadic diarrhoea. It is an important cause of water- and food-borne disease, day-care centre outbreaks, and illness in international travellers. The parasite occurs in two forms; cyst (infectious) and trophozoite forms.

### CLINICAL

- Giardiasis has a variable presentation:
  - 50% clear the infection in the absence of clinical symptoms
  - 5–15% shed the cysts asymptomatically
  - 35–45% have symptomatic infection
- Acute giardiasis typically presents with diarrhoea, steatorrhoea, and malaise and weight loss.
- Chronic giardiasis may follow the acute phase in up to half of symptomatic infections.

### DIAGNOSIS

- Stool microscopy should be performed to detect *Giardia* trophozoites and cysts which are excreted intermittently. *Giardia* can be detected in a single specimen in 50–70% of cases and in three specimens in up to 90% of cases.
- Stool antigen detection assays have greater sensitivity than stool microscopy and may be used in circumstances where microscopy cannot provide a definite diagnosis.
- PCR is increasingly being used to diagnose *Giardia* infections. Ampath offers a multiplex stool parasite PCR which detects *Entamoeba histolytica, Giardia lamblia* and *Cryptosporidium* species.

### TREATMENT

- Fluid and electrolytes replacement
- Antimicrobial therapy is indicated only if the patient is symptomatic

**GIARDIA: ANTIMICROBIAL THERAPY**

**ADULTS**

Metronidazole 2 g PO daily for 3 days

OR

Metronidazole 400 mg PO 8 hourly for 5 days

OR

Tinidazole 2 g PO as a single dose

OR

Albendazole 400 mg PO once daily for 5 days

**CHILDREN**

Metronidazole 15 mg/kg/day PO given 8 hourly for 5–7 days

OR

Tinidazole 50–75 mg/kg PO as a single dose

OR

Albendazole 400 mg PO once daily for 5 days (children > 2 years of age)

Albendazole 200 mg PO once daily for 5 days (children 1–2 years of age)

### TREATMENT OF RECURRENT DISEASE

Recurrent diarrhoea following *Giardia* treatment may be due to recurrent infection or antimicrobial resistance. Residual lactose intolerance and other small bowel absorptive deficiencies should be excluded.

**ANTIMICROBIAL THERAPY FOR RECURRENT GIARDIASIS**

A drug from a different class e.g. nitazoxanide 500 mg PO 12 hourly for 3 days if the initial drug was metronidazole or tinidazole

OR

A longer course of the original drug e.g. metronidazole for 10 days instead of 5 days

OR

A higher dose of the original drug (this approach is not well studied in children) e.g. increased metronidazole dose to 35 mg/kg/day

OR

Use a combination regimen e.g. albendazole **AND** metronidazole

## CRYPTOSPORIDIOSIS

*Cryptosporidium* is an intracellular protozoan parasite and with *Giardia*, it is among the most common enteric parasitic pathogen in humans. *C. parvum* is the main species responsible for clinical disease in humans and is responsible for:

- Diarrhoea and malnutrition in young children in developing countries
- Sporadic water-related outbreaks of self-limiting diarrhoea in immunocompetent hosts
- Chronic, life-threatening illness in immunocompromised patients, particularly those with HIV infection
- Diarrhoeal infections in countries with increased crowding and poor sanitation

#### CLINICAL

- *Cryptosporidium* can cause an asymptomatic infection, a mild diarrhoeal illness, or severe enteritis with or without biliary tract involvement.
- Immunocompromised hosts including HIV-infected patients with $CD4^+$ counts $< 100$ cells/μL are at risk of protracted and severe disease with significant wasting.
- Extra-intestinal manifestations in AIDS patients include cholecystitis, cholangitis, hepatitis, pancreatitis and respiratory involvement.
- The illness usually resolves without therapy in 10 to 14 days in immunologically healthy people and can persist or relapse after initial therapy.

#### DIAGNOSIS

- Stool microscopy. Microscopy can also be performed on duodenal aspirates, bile secretions, respiratory tract specimens and gastrointestinal tract biopsies.
- PCR testing on stool is now regarded as the diagnostic test of choice. Ampath offers a multiplex stool parasite PCR which detects *Entamoeba histolytica, Giardia lamblia* and *Cryptosporidium* species.

#### TREATMENT

#### IMMUNOCOMPETENT PATIENTS

- Immunologically healthy patients usually recover spontaneously within a few weeks and parasitologic cure occurs within a few months without any specific therapy.

#### HIV-INFECTED PATIENTS

- Initiation of antiretroviral therapy to reconstitute immunity is the most important component of therapy.
- Supportive therapy with fluids, anti-diarrhoeal agents and enteral or parenteral nutrition should be provided.
- Antimicrobial therapy (nitazoxanide, paromomycin or azithromycin) in addition to antiretroviral therapy may be given for persistent and severe diarrhoea, however there is limited evidence for the efficacy of these agents.

### BLASTOCYSTIS HOMINIS

There is controversy regarding whether *B. hominis* is a commensal or true pathogen. The estimated prevalence is 30–50% in developing countries and 5–10% in developed countries. The mode of transmission is not fully understood with faecal-oral transmission being postulated.

*Blastocystis* species are often found in association with other potential pathogens and reports suggest that the majority of patients with *Blastocystis* spp. in their stools have an alternative aetiology identified on further investigation.

#### CLINICAL

Symptoms associated with *Blastocystis* spp. include watery diarrhoea, abdominal cramps, bloating, flatulence, urticaria and fatigue.

#### DIAGNOSIS

Stool microscopy.

**TREATMENT**

- *Blastocystis* species cause a self-limiting infection, with cases resolving within three days without any specific therapy.
- Asymptomatic patients do not require treatment.
- Symptomatic patients should have stool microscopy to exclude other potential pathogens.
- If no other pathogen is identified, therapy for *Blastocystis* should be administered with observation for a clinical response (may be due to elimination of *Blastocystis* or another undetected pathogen).

**BLASTOCYSTIS: RECOMMENDED ANTIMICROBIAL THERAPY**

**ADULTS**

Metronidazole 750 mg PO 8 hourly for 5–10 days

OR

Cotrimoxazole 6 mg/kg TMP & 30 mg/kg SMX PO per day for 7 days

**CHILDREN**

Metronidazole 35 mg/kg/day PO divided into three doses for 5–10 days

## INTRA-ABDOMINAL INFECTIONS

Infections within the abdominal cavity typically arise because of inflammation or disruption of the gastrointestinal tract. Less commonly, they can arise from gynaecologic infection or urinary tract infection. Intra-abdominal infections (IAI) are usually polymicrobial and result in an intra-abdominal abscesses or secondary peritonitis, which may be generalised or localised (phlegmon). Intra-abdominal infections are diagnosed by routine history, physical examination and laboratory tests. Management of IAI includes fluid resuscitation, surgical intervention or drainage for source control and empiric antibiotic therapy.

### COMMUNITY-ACQUIRED IAI

**TREATMENT**

- Empiric therapy should be initiated once a diagnosis of IAI is made or suspected.
- Antibiotic therapy should be active against the enteric flora which includes enteric Gram-negative aerobic and facultative anaerobic bacilli, enteric Gram-positive cocci and obligate anaerobic bacilli.

**LOW-RISK COMMUNITY-ACQUIRED IAI IN PATIENTS WITHOUT RISK FACTORS FOR ANTIBIOTIC RESISTANCE OR TREATMENT FAILURE**

| | |
|---|---|
| **Single-agent regimens** | Ertapenem, piperacillin-tazobactam OR amoxicillin-clavulanate |
| **Combination regimens** | Cefazolin, cefuroxime, ceftriaxone, cefotaxime, ciprofloxacin OR levofloxacin, given in combination with metronidazole |

**HIGH-RISK COMMUNITY-ACQUIRED IAI IN PATIENTS WITH RISK FACTORS FOR ANTIBIOTIC RESISTANCE OR TREATMENT FAILURE**

| | |
|---|---|
| **Single-agent regimens**: | Imipenem-cilastatin, meropenem, doripenem, or piperacillin-tazobactam |
| **Combination regimens**: | Cefepime, ceftazidime, ciprofloxacin, or levofloxacin, given in combination with metronidazole |

- Antifungal therapy with an echinocandin in patients with severe community acquired IAI is recommended if there is growth of *Candida* spp. from a sterile site
- In neonates, empiric antifungal therapy should be started if *Candida* is suspected

## HEALTHCARE-ASSOCIATED IAI

Empiric therapy for healthcare-associated IAI should be driven by local microbiologic epidemiology as the likelihood of drug resistant organisms is high. Targeted antimicrobial therapy should then be chosen based on the results of culture and susceptibility testing from appropriate specimens.

**HEALTHCARE-ASSOCIATED IAI: EMPIRIC ANTIBIOTICS**

| | |
|---|---|
| **Single-agent regimens:** | Imipenem-cilastatin, meropenem, doripenem, or piperacillin-tazobactam |
| **Combination regimens:** | Cefepime or ceftazidime, administered together with metronidazole **AND** ampicillin OR metronidazole **AND** vancomycin<br>Duration of antibiotic therapy should be limited to 4–7 days, unless it is difficult to achieve source control |

Add the following to the above empiric regimens if necessary:
- To provide cover for enterococci: vancomycin or teicoplanin
- For patients known to be colonised with MRSA: vancomycin or teicoplanin
- Antifungal therapy with an echinocandin if there is growth of *Candida* spp. from a sterile site
- In neonates, empiric antifungal therapy should be started if *Candid*a is suspected: use an echinocandin or amphotericin B