Bacterial gastroenteritis

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Abstract

Infectious diarrhoea is a major public health concern worldwide. In developing countries it leads to around two million deaths per year in the under-five age group alone. In developed countries diarrhoeal disease is rarely fatal, except at extremes of age or in the immunocompromised; however, it remains a cause of significant morbidity. Gastroenteritis refers to syndromes of diarrhoea or vomiting resulting from non-inflammatory infection in the upper small bowel or inflammatory infection in the colon, caused by bacteria, viruses, or parasites. In approximately half of suspected cases, no causal agent is identified. The prevalence of each pathogen varies with geographical region and population factors. Viruses are more common in infants and children, particularly in developed countries. Bacteria, the focus of this review, are responsible for 10—55% of diarrhoeal episodes, with highest rates occurring in the developing world. However, with increase in international travel and globalization of the food industry, we must be alert to pathogens more typical of the developing world. Increasing antibiotic resistance must also be considered when choosing empirical treatment. Advances in molecular and rapid detection of enteric pathogens hold promise of improved therapeutic, preventative and control strategies, although widespread introduction of novel diagnostics into clinical practice will require careful cost-benefit analyses.

Keywords *Campylobacter*; diagnosis; diarrhoea; diarrhoeagenic *Escherichia coli*; gastroenteritis; management; pathogenesis; *Salmonella*; *Shigella*; *Vibrio cholerae*

Introduction

Infectious diarrhoea is a major public health concern worldwide. In developing countries it leads to around two million deaths per year in the under-five age group alone.[1] In developed countries diarrhoeal disease is rarely fatal, except at extremes of age or in the immunocompromised, where it remains a cause of significant morbidity.

Gastroenteritis refers to syndromes of diarrhoea or vomiting due to non-inflammatory infection in the upper small bowel or inflammatory infection in the colon, and may be caused by bacteria, viruses, or parasites. In approximately half of all suspected cases, no causal agent is identified. The prevalence of each pathogen varies with geographical region and population factors. Viruses are more common in infants and children, particularly in developed countries. Bacteria, the focus of this review, are responsible for 10—55% of diarrhoeal episodes, with highest rates occurring in the developing world. However, with increases in international travel and globalization of the food industry, we must be alert to cases of imported gastroenteritis caused by pathogens more typical of the developing world. Increasing antibiotic resistance must also be considered when choosing empirical treatment.

Advances in molecular and rapid detection of enteric pathogens have enhanced our understanding of the epidemiology of diarrhoeal disease and highlighted emerging infective agents. This knowledge holds promise of improved therapeutic, preventative and control strategies, although widespread introduction of novel diagnostics into clinical practice will require careful cost-benefit analyses.

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Epidemiology and risk factors

In the developing world, children under the age of five suffer from three or four diarrhoeal episodes per year resulting in 4.9 deaths per 1000 of this population.[1] Although mortality has declined with the introduction of oral rehydration therapy (ORT), morbidity remains unchanged and prolonged or recurrent diarrhoea is associated with malnutrition and adverse effects on growth and development. In developed countries, around 0.6 episodes occur per person per year, less than 1% being reported to general practitioners, and few cases being referred to hospital; however, acute diarrhoea results in 10,000 deaths annually in United States (US), as well as considerable morbidity and economic loss.[2,3]

Causative bacterial pathogens

UK Health Protection Agency surveillance data indicate that *Campylobacter* is the commonest cause of bacterial gastroenteritis, followed by non-Typhi salmonellae (NTS) and then *Shigella* species.[4] However, screening for diarrhoeagenic *Escherichia coli* strains other than *E. coli* 0157:H7 is not done routinely, and these strains probably contribute to an increasing burden of disease. *Campylobacter* is also the most common bacterial cause of investigated food-borne illness, accounting for 19.6%, with others being due to *Clostridium perfringens* (9.8%), *Yersinia* (7.5%), NTS (4.2%), and diarrhoeagenic *E. coli* (3.7%). It is of note that *E. coli* 0157:H7 and *Listeria* account for less than 0.1% of cases, but are responsible for 15% of deaths.[5] About 8% of diarrhoeal illness is travel-associated, with NTS and *Campylobacter* predominating from Europe and *Shigella* from travel to the Indian subcontinent and sub-Saharan Africa.[6] When polymerase chain reaction (PCR) methods are used to detect diarrhoeagenic *E. coli*, these strains exceed the usual culture-defined pathogens, being identified in up to 35% of cases compared to 12% of controls.[7,8] Enterotoxigenic *E. coli* (ETEC) is in fact the commonest cause of travellers' diarrhoea worldwide.

Risk factors[9]

Many host and environmental factors influence the development of bacterial gastroenteritis, including:

- *Weaning*: loss of mucosal immunity from maternal antibody increases susceptibility.

- *Age*: young children lack immunity to some pathogens, e.g. enteropathogenic *E. coli*. The elderly are at increased risk of infection due to age-related alterations in mucus production, gut flora, and cell surface receptors for microbial adhesions or toxins, e.g. *Clostridium difficile*.
- *Gastric acidity*: achlorhydria, gastrectomy, and use of antacids/proton pump inhibitors decrease the bactericidal effect of gastric acid.
- *Intestinal dysmotility* adversely affects the distribution of normal intestinal flora and prevents removal of pathogens.
- *Antibiotics* reduce normal intestinal flora (particularly anaerobes) thereby increasing colonization opportunities for pathogens.
- *Immunosuppression*: impaired adaptive immunity with human immunodeficiency virus (HIV) predisposes to some enteric pathogens, e.g. *Salmonella*.
- *Genetic predisposition*: blood group O is associated with increased susceptibility to cholera.
- *Overcrowded living conditions* enhance spread of organisms with a low infective dose, e.g. *Shigella*.
- *Poor sanitation* increases food and waterborne infection as well as person-to-person transmission.

Pathogenic mechanisms and associated clinical syndromes

Bacteria cause gastroenteritis by three main mechanisms associated with distinctive but overlapping clinical syndromes. Examples are shown in Table 1.

- *Production of preformed toxin* induces vomiting and abdominal cramps within a few hours of ingestion.
- *Secretion of toxin after adhering to intestinal epithelium* causes a syndrome of watery diarrhoea, without blood or mucus or associated fever (non-inflammatory).
- *Invasion of intestinal mucosa* causes dysentery, the passage of small-volume stools containing blood, mucus and pus associated with fever, lower abdominal pain and tenesmus (inflammatory).

Enteric fever is a distinct clinical syndrome caused by *Salmonella enterica* var. Typhi and Paratyphi, with distinct pathogenic mechanisms involving invasion of intestinal mucosa, migration to lymphatics and multiplication in the reticuloendothelial system. It causes a febrile illness with systemic upset and often bacteraemia. Gastroenteritis is not a common feature.

The molecular pathogenic mechanisms of gastrointestinal infection for the major bacterial pathogens are shown in Figure 1.[9,10]

Major bacterial causes of gastroenteritis and the most commonly associated clinical syndromes

Intoxication
- *Staphylococcus aureus*
- *Bacillus cereus*
- *Clostridium perfringens*

Watery diarrhoea
- *Vibrio cholerae*
- Non-Typhi salmonellae
- Enterotoxigenic *Escherichia coli*
- Enteropathogenic *Escherichia coli*
- *Clostridium perfringens*
- *Listeria monocytogenes*
- *Bacillus cereus*

Dysentery
- *Shigella* spp.
- Entero-invasive *Escherichia coli*
- Enterohaemorrhagic *Escherichia coli*
- *Campylobacter*
- *Yersinia*

Table 1

Principal bacterial causes of gastroenteritis

Campylobacter

Campylobacter jejuni is a common cause of bacterial gastroenteritis worldwide with children and young adults most susceptible. The bacterium resides in the intestine of cattle, poultry, domestic pets and birds. Infection occurs after ingestion of contaminated undercooked food, or close contact with infected animals. Person-to-person transmission is uncommon. The infective dose is between 10^2 and 10^5 organisms.

Clinical presentation varies, from an asymptomatic carrier state, to a mild enteritis with abdominal cramps and watery diarrhoea, to dysentery with severe abdominal pain, fever and bloody diarrhoea. The incubation period is 1–6 days, and there is often a prodrome of fatigue and myalgia. Symptoms last a few days but persist beyond a week in around 10% of cases. Important though uncommon complications include bacteraemia and osteomyelitis, particularly due to *Campylobacter fetus* in immunocompromised hosts. A few weeks after primary infection reactive arthritis may occur, and in less than one in 1000 cases, Guillain–Barré syndrome, caused by an autoimmune attack on peripheral nerves by host antibodies against *Campylobacter* lipo-oligosaccharides (LOS), which closely resemble human gangliosides. More recently, *Campylobacter* has also been linked to a rare form of lymphoma called immunoproliferative small intestinal disease (IPSID) which may respond to antimicrobial therapy in the early stages.[11]

Due to the recent dramatic increase in fluoroquinolone resistance worldwide, ranging from almost 50% in the UK[4] to 80% in parts of Asia,[12] azithromycin 500 mg daily for three days is the treatment of choice.

Diarrhoeagenic *E. coli*

E. coli is part of the normal gut flora, but at least five groups of pathogenic strains exist which cause a range of gastrointestinal illness.

- *Enteropathogenic (EPEC)* causes watery diarrhoea in infants in developing countries, and sporadic diarrhoea during the summer in industrialized countries. Humans are reservoirs, and transmission from person-to-person takes place as a result of overcrowded and unhygienic living conditions, or from contaminated infant feeds. Institutional outbreaks are common.
- *Enterotoxigenic (ETEC)* causes watery diarrhoea in developing countries, particularly young children, and is the commonest cause of travellers' diarrhoea. Humans are the reservoir of infection, and food and water contaminated by human faeces transmit infection. The infective dose is high (10^8 organisms).