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Diagnosis and management of acute enteropathogens in returning travelers

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Acute watery diarrhea is one of the leading causes of gastrointestinal illness in returning travelers (Figure 1). Acute diarrhea is generally defined as the passage of ≥3 unformed stools per 24 hours plus at least one additional symptom (e.g., nausea, vomiting, abdominal cramps, fever, blood/mucus in the stools, or fecal urgency) (Jiang and DuPont, 2017; Leung *et al.*, 2019; Ross *et al.*, 2013; Steffen, 2017). The clinically important acute enteropathogens include specific variants of *Escherichia coli* (including enterotoxigenic [ETEC] and enteroaggregative [EAEC] strains), *Vibrio cholerae* norovirus, rotavirus, *Cyclospora, Cryptosporidium, Campylobacter, Shigella*, and *Salmonella* (Table 1) (Jiang and DuPont, 2017; Leung *et al.*, 2019; Ross *et al.*, 2013; Steffen, 2017). Most cases go unreported, however, and patients are typically treated at home. The disease is usually self-limiting, with about half of patients spontaneously cured within 48 hours (Leung *et al.*, 2019; Ross *et al.*, 2013). However, in approximately 20% diarrhea persists, requiring further investigation and intervention (Leung *et al.*, 2019; Ross *et al.*, 2013).

What should I consider in my initial assessment?

In the initial assessment of a patient with acute diarrhea, a detailed history and physical examination are essential to determine the severity of dehydration (mild, moderate, or severe). The physician needs to carefully assess the patient's age (especially if <6 months), conscious state, capillary refill, skin turgor (retraction), respiratory rate, fluid intake, urine output, and body weight (>10% loss is severe) (Leung *et al.*, 2019; Ross *et al.*, 2013). Disease patterns vary greatly among countries, and within countries there can also be differences depending on environment, ecology, altitude, climate, vectors, and other factors (Ross *et al.*, 2013). Other useful information to obtain from the patient includes types of foods and liquids consumed, exposure to ill people, vaccination history, and medications taken (Ross *et al.*, 2013). A physician should also know the incubation periods of potential infections (Table 1). Acute clinical symptoms (appearing <7 days after exposure) could be indicative of enteric viral or bacterial infection, whereas chronic symptoms (appearing ≥14 days after exposure) may suggest an enteric protozoal or helminthic infection (Leung *et al.*, 2019; Ross *et al.*, 2013). Consideration of these factors, in combination with careful assessment of the timing of clinical signs and symptoms, should help the physician determine the appropriate laboratory test to order and whether empirical treatment should be initiated (Leung *et al.*, 2019; Ross *et al.*, 2013).

How do I make a diagnosis?

Current methods for detecting acute enteropathogens comprise stool and blood cultures, enzyme-linked immunosorbent assays (ELISAs), and polymerase chain reaction (PCR) (Leung *et al.*,

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Table 1
Acute enteropathgens and the returning traveler (Aliabadi et al., 2015, Al-Yousif et al., 2002, Bajait and Thawani, 2011, Centers for Disease Control and Prevention 2021, Churgay and Aftab, 2012, Das et al., 2016, DuPont, 2012, Francis, 2011, Giersing et al., 2019, Harris et al., 2012, Harro et al., 2019, Huq et al., 2012, Jiang et al., 1992, Li et al., 2020).

Acute Enteropathogen		Areas of High Risk	Mode of Transmission	Incubation Period	Common Symptoms	Diagnostic Method	Adult Treatment	Pediatric Treatment	Vaccine
Escherichia coli ETEC EAEC EIEC		South Asia, South East Asia, Middle East, Afica, Latin America, South America	Dairy products, uncooked meats, tap water	3-4 days	Diarrhoea, fever, abdominal pain, vomiting, nausea 'yellow watery stools'	Stool culture	Ciprofloxacin, 750 mg/day x 3 days or Azithromycin 1 g as single dose	Azithromycin 10 mg/kg/day x 3 days or Ceftriaxone 50 mg/kg/day od x 3 days	Dukoral OCV is given to travellers 7 days before departure
Vibrio cholerae		South Asia, South East Asia, Middle East, Afica, Caribbean	Fecal-oral, tap water, seafood, human contact	1-5 days	Diarrhoea, fever, abdominal pain, vomiting, nausea 'rice water stool'	Stool culture	ORS + Zn Doxycycline, 300 mg single dose or Azithromycin 1 g single dose	ORS + Zn Doxycycline 2 mg/kg single dose or Azithromycin 20 mg/kg	Shanchol OCV two-doses 14 days apart) Euvichol OCV two-doses 14 days apart) Dukoral OCV two-dose regimen (7 days apart)
Norovirus		Worldwide	Fecal-oral, human contact, respiratory	1-2 days	Diarrhoea, fever, abdominal pain, vomiting, nausea	PCR assay	Rehydration	Rehydration	Vaccines using virus-like particles is under development
Rotavirus		Worldwide	Faecal-oral	2 days	Fever, vomiting, diarrhoea 'yellow watery stools'	EIA, latex agglutination	Rehydration ORS	Rehydration ORS	Rotarix two-doses at 2 and 4 months Rotateq three-doses at 2, 4 and 6 months Rotavac three-doses at 2, 4 and 6 months Rotasiil three-doses at 6, 10, and 14 weeks
Crytosporidium		South Asia, South East Asia, Middle East, Afica, Oceania, Europe	Faecal-oral, uncooked foods, tap water	1-12 days	Fever, vomiting, diarrhoea, headache	PCR assay	Nitazoxanide, 500 mg twice a day for 3 days	Nitazoxanide 100-200 mg twice a day for 3 days	No vaccine is available
Cyclospora		South Asia, South East Asia, Middle East, Afica, Latin America, South America	Faecal-oral	7 days	Diarrhoea, fever, abdominal pain, myalgia	PCR assay Acid-fast staining	Trimethoprim, 160 mg Sulfamethoxazole 800 mg twice a day for 3 days	Trimethoprim 4 mg/kg Sulfamethoxazole 20 mg/kg twice a day for 3 days	No vaccine is available

(*continued on next page*)

Table 1 (*continued*)

Acute Enteropathogen		Areas of High Risk	Mode of Transmission	Incubation Period	Common Symptoms	Diagnostic Method	Adult Treatment	Pediatric Treatment	Vaccine
Campylobacter		South Asia, Southest Asia	Poultry, milk, tap water	1-4 days	Acute watery diarrhoea, fever	Stool culture	Azithromycin, 500 mg/day for 3 days	Azithromycin 10 mg/kg/day for 3–5 days	C. jejuni capsular polysaccharide conjugate vaccine (under development)
Shigella		North Africa, South Asia Southeast Asia, Oceania	Human contact, food, tap water	1-8 days	Severe diarrhea, dysentery, fever	Stool culture	Ciprofloxacin, 500 mg twice a day for 3 days	Azithromycin, 10 mg/kg/day for 3 days	Shig. flexneria 2a conjugate (SF2a-TT15) vaccine *Shig. sonnei (WRSS1) live attenuated vaccine* (both under development)
Salmomella Serovar Typhi		South Asia, Africa	Human contact, food, tap water	5-14 days	Fever, headache, malaise, abdominal pain, diarrhea	Blood and stool culture	Ciprofloxacin, 20 mg/kg/day for 7 days; or azithromycin, 20 mg/kg/day for 7 days	Ciprofloxacin, 20 mg/kg/day for 7 days; or azithromycin, 20 mg/kg/day for 7 days	Typbar-TCV® single dose conjugate vaccine PedaTyph™ single dose conjugate vaccine Vi polysaccharide (ViPS) single dose vaccine Ty21a four-dose live oral vaccine on day 1,3, 5, 7
Nontyphoidal		Southeast Asia, Oceania	Poultry, egg, meat	8-24 hours	Fever, headache, malaise, abdominal pain, diarrhea	Blood and stool culture	Ciprofloxacin, 20 mg/kg/day for 7 days; or azithromycin, 20 mg/kg/day for 7 days	Ciprofloxacin, 20 mg/kg/day for 7 days; or azithromycin, 20 mg/kg/day for 7 days	

Note: All figures were obtained from public domain. ORS + Zn = oral rehydration solution + Zinc.

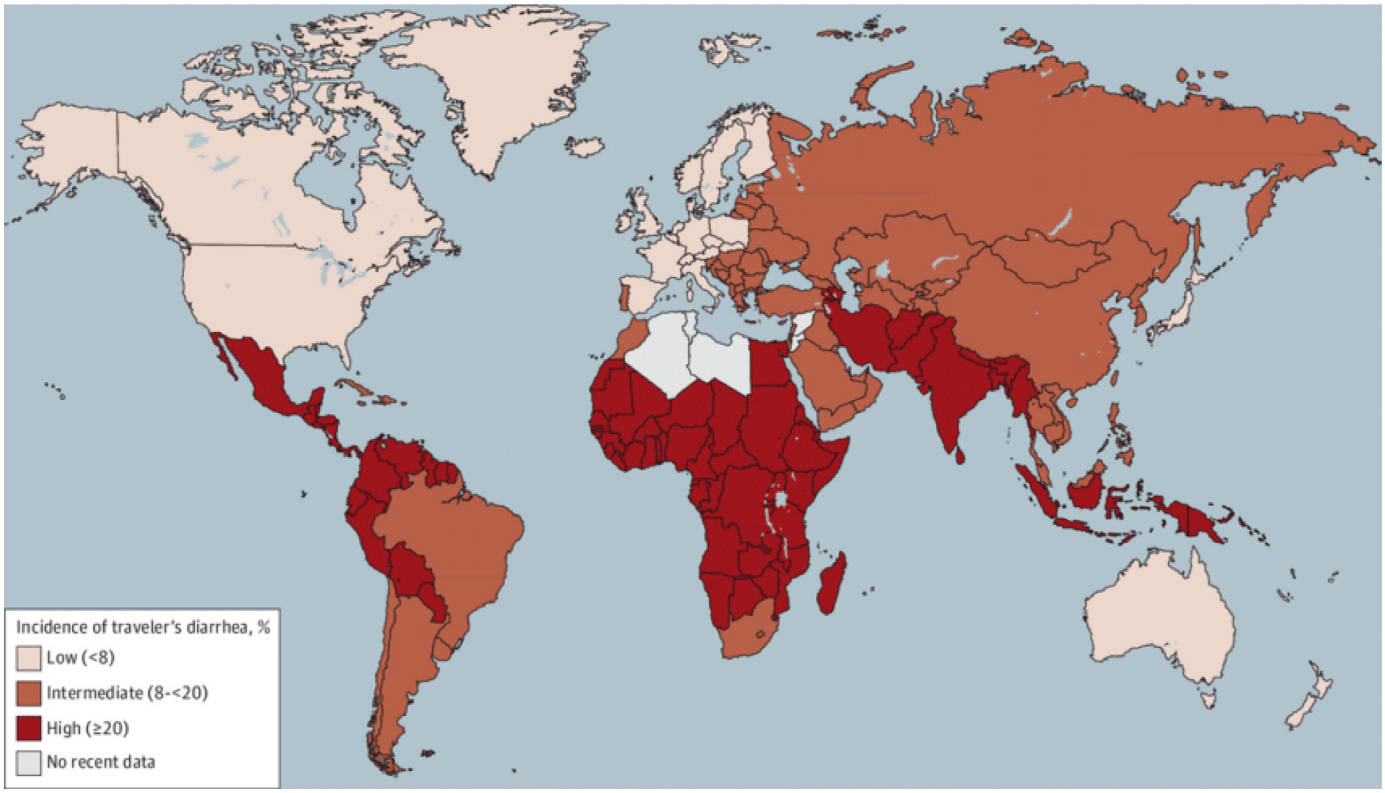

Figure 1. Global incidence of traveler's diarrhea. Note: figure obtained from the public domain.

2019; Ross *et al.*, 2013). Modern PCR approaches detect bacterial, viral, and protozoal pathogens with high sensitivity and specificity, but technical skills and equipped laboratories are required. Table 1 lists the diagnostic methods commonly used for select acute enteropathogens (Leung *et al.*, 2019; Ross *et al.*, 2013).

There is no single method available for the diagnosis of all six pathogenic strains of *E. coli* (Croxen *et al.*, 2013). Additional morphologic, typing, biochemical, phenotypic, and genotypic analysis is required for identification and confirmation of the specific pathotypes (Croxen *et al.*, 2013). Currently, molecular techniques are preferred for more rapid detection and identification (Croxen *et al.*, 2013). Fresh stool, rectal swabs, or surgical specimens are collected and transferred in buffered glycerol or Cary-Blair transport medium (Croxen *et al.*, 2013). For phenotypic detection of pathogen, the stool is examined in selective media with biochemical assays. Infection of cultured cells is determined through cytotoxicity assays, fluorescent staining, and adherence pattern assays (Croxen *et al.*, 2013). Molecular detection is based on PCR, microarray, or enzyme-linked immunoassay (Croxen *et al.*, 2013). Various typing methods, such as O- and H-antigen serotyping, multilocus sequence typing, ribotyping, pulsed-field gel electrophoresis, and multiple-locus variable-number tandem repeat analysis are used (DebRoy *et al.*, 2011; Noller *et al.*, 2003; Wang *et al.*, 2003).

Clinically distinguishing cholera in a patient infected with another enteric pathogen that causes acute watery diarrhea is very difficult without laboratory testing (Harris *et al.*, 2012; Learoyd and Gaut, 2018). Stool culture is the gold-standard diagnostic method for the isolation and identification of *Vibrio cholerae* serogroup O1 or O139 (Huq *et al.*, 2012; Ramamurthy *et al.*, 2020). Proper sample collection (stool/rectal swabs) and transportation to the laboratory is the key to increasing the efficacy of the test (Huq *et al.*, 2012; Ramamurthy *et al.*, 2020). Cary-Blair is the preferred transport medium for sample transportation from field settings to the laboratory, and selective thiosulfate-citrate-bile salts agar or taurocholate-tellurite-gelatin agar is preferred for isolation and identification (Huq *et al.*, 2012; Ramamurthy *et al.*, 2020). PCR is another sensitive method for the diagnosis of cholera, but improved laboratory capacity is required for performing such a test (Huq *et al.*, 2012; Ramamurthy *et al.*, 2020).

Rotavirus can be detected in stool samples of patients with gastroenteritis through antigen-based ELISAs and immunochromatographic assays. These tests have high sensitivity and specificity (90-95%) (Parashar *et al.*, 2013). Rotavirus strain characterization can be performed using reverse transcriptase-PCR (RT-PCR) to identify both G and P types (Kang *et al.*, 2004). In addition, a rapid chromatographic immunoassay for the qualitative detection of rotavirus in human stool specimens can be used for rapid detection (Al-Yousif *et al.*, 2002). The test is based on antibodies specific to rotavirus and gives results in 10 min (Al-Yousif *et al.*, 2002). As for rotavirus, ELISA and RT-PCR are commonly used to detect norovirus in either stool or vomit specimens (Patel *et al.*, 2009). The sensitivity of the test depends on viral load and detection capacity for various genetic subtypes (Patel *et al.*, 2009). Because of a lack of accurate diagnostic methods and lack of available facilities in most developing countries, it is difficult to determine the true burden of disease (Patel *et al.*, 2009).

The laboratory diagnosis of cryptosporidiosis is performed microscopically by detection of oocysts in stool samples using various techniques such as acid-fast staining, direct fluorescent antibody, and/or enzyme immunoassay for detection of *Cryptosporidium* spp. antigens (Smith, 2007). The detection of oocysts in the stool is difficult; hence, fecal samples should be collected on three separate days and examined microscopically (Smith, 2007). In reference diagnostic laboratories, PCR is widely used as the gold standard to identify *Cryptosporidium* at the species level, although this method is rather expensive (Smith, 2007).

Campylobacter, Shigella, and *Salmonella* are routinely detected using stool or blood culture (Table 1). Microarray on digital ver-

satile disc is now being used for identification and genotyping of *Salmonella* and *Campylobacter* in meat products (Tortajada-Genaro *et al.*, 2015). In patients with bloody diarrhea, stool culture and fecal toxin assay with commercial ELISAs are recommended (DuPont, 2009).

What should be my management strategy?

Management will depend on the severity of dehydration and the organism identified or suspected (Ross *et al.*, 2013; Steffen, 2017). Fluid replacement is critical in patients with profuse watery diarrhea and dysentery.Antibiotics play an important role in shortening the duration, frequency, and severe complications of bacterial diarrhea (Ross *et al.*, 2013; Steffen, 2017). Currently, the treatment includes the macrolide azithromycin, the third-generation cephalosporin ceftriaxone, and the fluoroquinolone ciprofloxacin (Table 1) (Ross *et al.*, 2013; Steffen, 2017). Mild cases of enteroinvasive *E. coli* (EIEC) are self-limiting, but sometimes this pathogen causes severe symptoms (mimicking shigellosis) that require antibiotic treatment (Croxen *et al.*, 2013). ETEC can cause severe diarrhea; intravenous rehydration may be necessary (Croxen *et al.*, 2013). Antisecretory drugs such as loperamide, along with antibiotics such as fluoroquinolones, azithromycin, and rifaximin, can lessen the duration of infection and are commonly used in self-treatment (Croxen *et al.*, 2013; Ross *et al.*, 2013). Enteropathogenic *E. coli* (EPEC) shows a high degree of multidrug resistance to recommended antibiotics (Croxen *et al.*, 2013). However, adherent-invasive *E. coli* (AIEC) can be treated with a wide range of antibiotics (e.g., ciprofloxacin or fluoroquinolones) (Croxen *et al.*, 2013). Recently, yeast-based probiotics have also been used. Diffusely adherent *E. coli* (DAEC) is susceptible to nalidixic acid, ceftazidime, gentamicin, lomefloxacin, and ofloxacin. Zinc and nutritional therapy are also beneficial for treating *E. coli* diarrhea (Croxen *et al.*, 2013).

Rapid assessment and management of dehydration are crucial for cholera management, and the treatment plan is chosen according to dehydration status (Davies *et al.*, 2017; Pietroni, 2020; Sousa *et al.*, 2020). Patients with some signs of dehydration can be effectively treated with oral rehydration solution (ORS) (Davies *et al.*, 2017; Pietroni, 2020; Sousa *et al.*, 2020). Patients with severe dehydration need immediate intravenous fluid replacement with 100 ml/kg during a 3-hour administration period (Davies *et al.*, 2017; Pietroni, 2020; Sousa *et al.*, 2020). One-third of the total volume should be given in the first 30 minutes (Davies *et al.*, 2017; Pietroni, 2020; Sousa *et al.*, 2020). For children <1 year of age, the volume replacement plan is for administration during a 6-hour period (30 ml/kg in the first hour and 70 ml/kg in subsequent 5 hours) (Davies *et al.*, 2017; Pietroni, 2020; Sousa *et al.*, 2020). Ringer's lactate solution (sodium chloride, sodium lactate, potassium chloride, and calcium chloride) and cholera saline (sodium chloride, potassium chloride, and sodium acetate) are the intravenous fluids commonly used for the management of cholera (Davies *et al.*, 2017; Pietroni, 2020; Ross *et al.*, 2013; Sousa *et al.*, 2020). According to the World Health Organization (WHO) guideline, antibiotics should be used only in patients with severe dehydration (Pietroni, 2020). The choice of antibiotic should be based on availability and local antibiotic susceptibility (Davies *et al.*, 2017; Pietroni, 2020; Sousa *et al.*, 2020). The antibiotic options include macrolides, fluoroquinolones, and tetracycline (Davies *et al.*, 2017; Pietroni, 2020; Sousa *et al.*, 2020). However, a single dose of azithromycin (1 g for adults or 20 mg/kg for children) is effective for the treatment of cholera (Saha *et al.*, 2006). According to Saha *et al.* (2006), "Patients who were treated in a clinical trial with azithromycin had a shorter duration of diarrhea than did patients treated with ciprofloxacin (median, 30 vs 78 hours); a lower frequency of vomiting (43% vs 67%); fewer stools (median, 36 vs 52); and a lower stool volume (median, 114 vs 322 ml/kg of body weight)". Supplementation with vitamin A (VAS) and zinc can reduce the duration and severity of diarrhea in children up to 5 years of age (Bajait and Thawani, 2011; Francis, 2011). The findings from a systematic review by Imdad et al. (2010) included 43 studies and 230,354 children (Francis, 2011). VAS led to a 24% reduction in all-cause mortality (risk ratio 0.76 [95% CI 0.69, 0.83]) (Francis, 2011). The benefits of VAS were strongest in high-risk populations (Francis, 2011). Approximately one death was prevented for every 45 children who received the supplement (Francis, 2011).

Most rotavirus cases are self-limiting (Crawford *et al.*, 2017). Severe dehydration in children becomes life-threatening if not treated (Crawford *et al.*, 2017). Rehydration can be performed with hypo-osmolar oral rehydration salts or, in patients with severe dehydration or vomiting, with intravenous fluids (Crawford *et al.*, 2017). Continuation of regular diet and adequate fluid intake are recommended for children with minimal or ongoing dehydration (Crawford *et al.*, 2017). Treatment with probiotics has a positive immunomodulatory effect that improves intestinal function in children and might decrease the episodes of diarrhea (Das *et al.*, 2016; Sindhu *et al.*, 2014). In a recent trial of 124 children with diarrhea (82 rotaviral and 42 cryptosporidial), baseline and clinical parameters were comparable between children receiving *Lactobacillus rhamnosus* GG (LGG) and placebo (Sindhu *et al.*, 2014). At the end of follow-up, fewer children with rotaviral diarrhea on LGG had repeated diarrheal episodes (25% vs 46%; $P = .048$) and impaired intestinal function (48% vs 72%; $P = .027$) (Sindhu *et al.*, 2014). In settings with evidence of mortality, zinc supplementation has been shown to be effective in reducing the duration and severity of diarrhea (Telmesani, 2010). A pooled analysis of randomized controlled trials of zinc supplementation performed in nine low-income countries in Latin America and the Caribbean, South and Southeast Asia, and the Western Pacific demonstrated that supplemental zinc led to an 18% reduction in the incidence of diarrhea and a 25% reduction in the prevalence of diarrhea (Telmesani, 2010). Norovirus patients are treated in a similar manner (Churgay and Aftab, 2012). Patients are given supportive treatment for diarrhea along with adjunctive treatments such as antiemetics, analgesics, and antimotility agents (Churgay and Aftab, 2012; Thorne *et al.*, 2016). Rehydration with ORS or intravenous fluids is sometimes performed in patients who are moderately or severely dehydrated (Churgay and Aftab, 2012; Thorne *et al.*, 2016).

Most patients with cryptosporidiosis recover within 2 weeks without treatment. However, immunocompromised patients recover more slowly, and the disease can be life-threatening in a subset of patients (Li *et al.*, 2020; Sparks *et al.*, 2015). The management of patients is usually with fluid and electrolyte therapy (e.g., sodium, potassium, and calcium), antimotility drugs (e.g., loperamide), and supplemental zinc (Li *et al.*, 2020; Sparks *et al.*, 2015). The antiparasitic drug nitazoxanide can help relieve diarrhea by targeting the parasite (Li *et al.*, 2020; Sparks *et al.*, 2015). To reduce viral load and boost immune response in patients who are immunocompromised with HIV/AIDS, antiretroviral therapies are required (Li *et al.*, 2020; Sparks *et al.*, 2015). Trimethoprim-sulfamethoxazole (TMP-SMX) is a combination drug used to treat patients with *Cyclospora* infection (Li *et al.*, 2020). TMP 160 mg/SMX 800 mg for adults and TMP 4 mg/SMX 20 mg per kg body weight for pediatric patients, twice daily for 3 days, are recommended (Li *et al.*, 2020).

For *Campylobacter* and *Shigella*, antimicrobial therapy is indicated (Table 1). For nontyphoidal *Salmonella*, antibiotics are given to patients in whom bacteremic disease is suspected (DuPont, 2012). Multidrug-resistant *Salmonella* serovar Typhi and *Salmonella* serovar Paratyphi are common in Asia and Sub-Saharan

Africa, and there are increasing reports of reduced susceptibility to fluoroquinolones (Meiring *et al.*, 2021). *Campylobacter jejuni* resistance to fluoroquinolones has become a concern in Southeast Asia, with rates of resistance of 80% reported in Thailand (Sproston *et al.*, 2018; Whelan *et al.*, 2019). Multidrug resistance in a distinct genotype of *Salmonella* serovar Typhimurium (ST313) has also emerged in Africa (Van Puyvelde *et al.*, 2019).

What vaccines are currently available?

Currently, vaccines are available against EPEC, DAEC, AIEC, and EIEC. Studies have shown that breast milk contains antibodies against EPEC and protects infants from diarrhea (Cravioto *et al.*, 1991; Parissi-Crivelli *et al.*, 2000). For Shiga toxin-producing *E. coli*, vaccines are being developed in mice and cattle (Fingermann *et al.*, 2018). ETEC vaccines containing heat-labile toxins exert protection against EAEC (Sack *et al.*, 2007). Because of the diverse strains of the ETEC pathogen, vaccines based on various formulations are being produced; these include live attenuated, inactivated whole-cell, hybrid toxin-producing, and fimbrial antigen-containing vaccines (Sack *et al.*, 2007). The Dukoral oral cholera vaccine, composed of the B subunit of cholera toxin (CTB), provides short-term protection against ETEC diarrhea in travelers (Table 1). An oral inactivated vaccine with recombinant CTB (rCTB) and a mix of major colonization factors (CFs), rCTB-CF ETEC, has been studied and found to result in decreased severity of diarrhea when compared with placebo among vaccinated travelers (Sack *et al.*, 2007). A live attenuated ETEC vaccine, ACE527, when coadministered with the mucosal adjuvant double-mutant heat-labile toxin, showed strong protection (Harro *et al.*, 2019). A phase I/II clinical trial, conducted on the oral whole-cell inactivated ETEC vaccine ETVAX, showed that the vaccine was safe and immunogenic among all age groups in Bangladesh (Qadri *et al.*, 2020). To date, however, there is no licensed vaccine available for protection against ETEC diarrhea.

Vaccination is considered the most effective way to prevent rotavirus infection among children. Currently, two WHO-prequalified vaccines are available globally: ROTARIX (GlaxoSmithKline Biologicals) and RotaTeq (Merck & Co., Inc.). RotaTeq is a live attenuated pentavalent vaccine that should be given orally in three doses at 2, 4 and 6 months of age. ROTARIX is a live attenuated monovalent vaccine that should be given orally in two doses at 2 and 4 months of age (Table 1) (Centers for Disease Control and Prevention, 2021). The efficacy of RotaTeq was 98% in protection against severe rotavirus gastroenteritis and 74% in protection against gastroenteritis of any severity. ROTARIX gives 85-96% protection against severe rotavirus gastroenteritis among children from the “developed” world (Europe, USA) (WHO, 2009). Two new rotavirus vaccines, ROTAVAC (Bharat Biotech, Hyderabad, India) and ROTASIIL (Serum Institute of India Pvt. Ltd., Pune, India), are now WHO-prequalified (Skansberg *et al.*, 2020). The WHO recommends using the rotavirus vaccine in national immunization programs in South and Southeast Asia and in Sub-Saharan Africa (WHO, 2013). Viral diversity and short duration of immunity against the emerging genogroups of norovirus are major obstacles in vaccinating people against the virus (Parrino *et al.*, 1977). However, several vaccines using virus-like particles are currently in preclinical development (Jiang *et al.*, 1992; Johnson *et al.*, 1990). Clinical trials examining various routes of administration (e.g., intranasal, oral, and intramuscular) are ongoing (Aliabadi *et al.*, 2015; Giersing *et al.*, 2019). There is currently no licensed vaccine for protection against cryptosporidiosis.

Three vaccines to protect against typhoid fever are licensed in the United States: a live attenuated strain Ty21a vaccine; a parenteral Vi capsular polysaccharide vaccine; and a parenteral killed whole-cell vaccine (Khanam *et al.*, 2022; Pasetti *et al.*, 2011). A *C. jejuni* capsular polysaccharide conjugate vaccine, a *Shigella flexneri* 2a conjugate vaccine (SF2a-TT15), and a *Shigella sonnei* live attenuated vaccine (WRSS1) are in various stages of development (Riddle and Guerry, 2016; Sarker *et al.*, 2021; van der Put *et al.*, 2022).

Further educational resources for professionals

- WHO. Diarrhea.

  https://www.who.int/health-topics/diarrhoea#tab=tab_1

- Centers for Disease Control and Prevention. Guidelines for the management of acute diarrhea after a disaster.

  https://www.cdc.gov/disasters/disease/diarrheaguidelines.html

- World Gastroenterology Organisation. Acute diarrhea in adults and children: a global perspective.

  https://www.worldgastroenterology.org/guidelines/acute-diarrhea/acute-diarrhea-english

Contributors' Statement

All authors contributed to writing the article and approved the final submission.

Declarations of competing interest

The authors have no competing interests to declare.

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