Tropical Bacterial Gastrointestinal Infections

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KEYWORDS

• Tropical infections • Diarrhea • Enteric fever • Cholera • *Salmonella* • *Shigella* • Antimicrobial resistance • Enteric vaccines

KEY POINTS

- Bacterial gastrointestinal infections are prevalent in tropical regions. Recent literature shows a rise in incidence of cholera, which is further augmented by natural disasters.
- Epidemiological trends suggest increasing rates of enteric fever in several endemic regions. In such areas vaccination of high risk populations with *S Typhi* vaccines is recommended.
- Invasive non-typhoidal Salmonellae infections are associated with high HIV incidence in Africa.
- The most common etiology for traveler's diarrhea is Enterotoxigenic strain of *E coli* (ETEC), reflecting the excessive burden of ETEC diarrheal disease in tropical regions.
- Antimicrobial resistance amongst enteric pathogens varies both geographically and temporally. Current resistance information is needed to develop updated antibiotic policies and guidelines.

BURDEN OF GASTROINTESTINAL DISEASES

Climatic and socioeconomic conditions in tropical and subtropical regions predispose to high gastrointestinal infection and diarrheal disease rates. Data from travel clinics and GeoSentinel are a testament to tropical countries being the highest-risk perpetrators of travel-related gastrointestinal infections (**Fig. 1**).[1] The true extent and burden of tropical gastrointestinal disease is, however, difficult to determine. Limited access to health care together with paucity of registries and published reports means that calculated disease rates from these regions are usually based on estimates. Gastrointestinal

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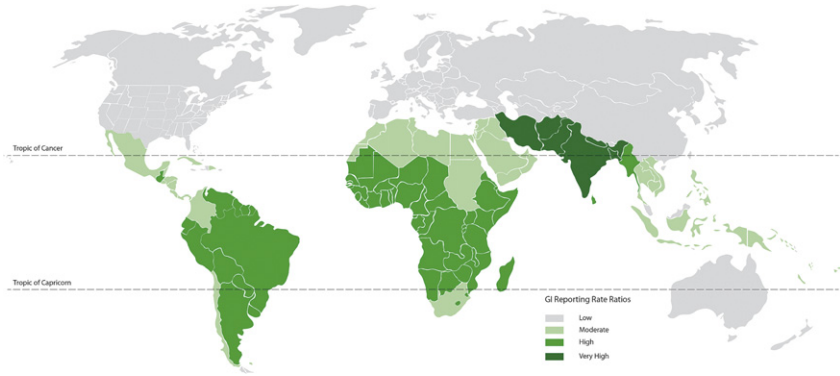

Fig. 1. A profile map of relative rates of acquisition of gastrointestinal infection by destination. Global distribution of reporting rate ratios for all gastrointestinal infections in travelers presenting to 30 GeoSentinel clinics on 6 continents. Twenty-eight countries with available country-specific data are outlined. Where country-specific data are lacking, a country assumes the characteristics of its region. (*Adapted from* Greenwood Z, Black J, Weld L, et al. Gastrointestinal infection among international travelers globally. J Travel Med 2008;15:221; with permission.)

diseases are recognized to exact considerable morbidity and mortality, particularly in children in whom long-term consequences on growth and development are well documented.[2–4] Epidemiology of common tropical bacterial gastrointestinal infections (**Table 1**) indicates that a considerable burden of these infections is due to cholera, salmonellosis, shigellosis, campylobacteriosis, and diarrheagenic *Escherichia coli* (DEC).[31] This review therefore focuses on these high-burden bacterial gastrointestinal infections.

In 2007, 177,963 cases of cholera were reported to the World Health Organization (WHO) from 53 countries, although the actual number of cases is estimated to be much higher.[32] Pandemics of cholera have plagued tropical and subtropical regions involving complex transmission events. The ongoing seventh cholera pandemic caused by *Vibrio cholerae* serotype O1, biotype El Tor originated in the Bay of Bengal (**Fig. 2**).[33,34] In addition, a new strain of *V cholerae*, serotype O139, which also emerged in the Bay of Bengal in 1992, continues to cause epidemics in the South Asia.[33] Several tropical countries have become endemic for cholera.[33] Recent literature shows an increase in incidence further augmented by an increase in natural disasters in tropical regions.[5–13]

Enteric fever is a systemic illness caused by *Salmonella enterica* serotypes Typhi and Paratyphi A, and less commonly by serotypes Paratyphi B and Paratyphi C. Humans are the only natural hosts and reservoirs. More than 21 million cases of typhoid and more than 5 million cases of paratyphoid fever are estimated to have occurred in the year 2000.[35] While enteric fever is a global health concern, the major brunt of morbidity and mortality are borne by tropical regions, especially South Asia.[36,37] Although attempts to measure true incidence of disease are hampered by limited availability of accurate diagnostic tests,[37] recent epidemiologic trends show an increase in rates of enteric fever in endemic regions including Indonesia, India, and Pakistan.[38] In Latin America, however, rates of enteric fever have declined in line with economic development and improved hygiene.[36]

Nontyphoidal Salmonellae (NTS), responsible for sporadic cases and outbreaks of foodborne diarrhea, are zoonotic in etiology. Globally, NTS are estimated to cause

93,757,000 cases of gastroenteritis annually, resulting in 155,000 deaths.[21] Although most disease is self-limiting, invasive infections are a prominent feature of NTS infection in the immunocompromised. The greatest impact of invasive NTS disease is seen in Africa, associated with a high incidence of human immunodeficiency virus in the region.[22] The incidence of invasive salmonellosis appears to be much lower in Asia.[23]

Bacillary dysentery caused by *Shigella* spp is another serious gastrointestinal infection. Four species (*dysenteriae*, *flexneri*, *boydii*, and *sonnei*) and 48 serotypes are prevalent.[39] Global burden estimates of shigellosis put the incidence at 80 to 165 million episodes annually, with 99% of these occurring in the developing world.[39] As much as 60% of bacterial dysentery cases in the tropics are caused by *Shigella flexneri.*[39] However, regional differences exist, for example in Thailand, where *Shigella sonnei* is the commonest isolated species.[39] A recent review estimates that approximately 125 million cases of shigellosis occur annually in Asia, of which some 14,000 are fatal.[40]

Another cause of significant morbidity in the tropics is campylobacteriosis, both intestinal and extraintestinal. The epidemiology of *Campylobacter* infections is similar to that of NTS.[41] Whereas *Campylobacter* spp are the commonest cause of bacterial gastroenteritis in the developed world,[42] in the tropics most cases occur in children younger than 5 years.[43]

The most common cause of traveler's diarrhea is the enterotoxigenic strain of *E coli* (ETEC), reflecting the excessive burden of ETEC diarrheal disease in tropical regions.[24] Other serotypes of diarrheagenic *E coli* (DEC) also occur in the tropics along with enteropathogenic *E coli* (EPEC), enteroaggregative *E coli* (EAEC), and diffusely adherent *E coli* (DAEC), causing outbreaks of infantile diarrhea.[24] Enteroinvasive *E coli* (EIEC) causes an illness similar to shigellosis.[24] Enterohemorrhagic *E coli* (EHEC) is associated with serious invasive and noninvasive disease. Toxic dysentery syndromes, however, are relatively uncommon in the tropics apart from a few areas that report high incidence.[24] The low incidence in this case may be attributable to limited access to diagnostic facilities preventing adequate and timely diagnosis of these pathogens.

THE DIAGNOSIS OF BACTERIAL GASTROINTESTINAL INFECTIONS: ARE TROPICS ANY DIFFERENT?

Diagnosis of gastrointestinal infections may be syndromic or etiologic. Common clinical features associated with these infections are shown in **Box 1**.

Most diarrheal syndromes are self-limiting, and culture-based testing is therefore not necessary for therapeutic purposes. The need for diagnostic evaluation arises in the following situations: severe disease or immunocompromised status, illness lasting more than 1 week, or illness associated with systemic symptoms.[44,45] From a public health perspective, however, diagnostic testing is required whenever an outbreak is suspected.[45]

DIAGNOSTIC TESTS

Stool Culture

Despite the turnaround time of 3 to 5 days, stool culture and sensitivity testing remain a gold standard for the diagnosis of bacterial diarrhea. Selective media are used to inhibit normal flora and detect Salmonellae, Shigellae, Vibrionaceae, *Campylobacter*, and toxigenic *E coli*. Culture-based diagnosis of gastroenteritis provides guidance for antimicrobial usage, and generates important microbial surveillance and resistance data.[46]

Table 1
Common tropical bacterial gastrointestinal pathogens

Pathogens Associated with Recently Reported Outbreaks (Last 5 Years)					
Pathogens	**Prevalent Species/ Serotype**	**Region**	**Countries Reporting Outbreaks**	**Year(s)**	**Reported Risk Factors for Outbreaks**
Vibrio cholerae	O1 biotype El Tor (serotypes I = Inaba, O = Ogawa)	Africa, Asia, South and Central America	Papua New Guinea[5]	2009–2010	Seasonal (El Nino)
			Central Africa[6]	2010	Seasonal factors
			Haiti[7]	2010	Earthquake
			Pakistan[8]	2010	Floods and IDPs
			Zimbabwe (O, I)[9]	2008–2009	Influx of refugees
			Iraq (I)[10]	2007	Probable sewage contamination of drinking water
			Vietnam[11]	2007–2008	
			India[12]	2009	Cyclone AILA
	O139	Asia	China (Sichuan province)[13]	2009	Consumption of soft-shelled turtles
Typhoidal Salmonellae (*Salmonella enterica* serotypes)	Typhi	Asia Africa South and Latin America	India (West Bengal)[14]	2007	Foodborne with a waterborne secondary wave
			Pakistan[15]	2009	Drinking water contamination
Shigella spp	*S flexneri* *S sonnei* *S dysenteriae* *S boydii*	Asia Africa Latin America	Brazil[16]	2007–2008	Multiple foodborne outbreaks
			Iran[17]	2007	Prison outbreak through contaminated raw vegetables
			Taiwan[18,19]	2007	Groundwater contamination
				2008	Psychiatric ward cross-transmission
Campylobacter spp		Africa Asia South America	Korea[20]	2009	Undercooked chicken

Pathogens endemic in tropics but not reported in recent outbreaks			
			Associated factors
Nontyphoidal Salmonellae		Africa, South America, Asia[21–23]	Common as etiology of self-limiting diarrhea, no recently reported outbreaks
Diarrheagenic *E coli* (DEC)	ETEC EPEC EIEC EHEC EAEC	Asia, South America, Africa[24]	Cause traveler's diarrhea, and outbreaks in infants; no recently reported well-characterized outbreaks
Mycobacterium tuberculosis		Asia, West Africa, Caribbean[25,26]	Gastrointestinal presentation increasingly reported. Likely to coexist with pulmonary tuberculosis, which tends to cluster and is highly infectious
Helicobacter pylori		Asia, Africa, South Amercia[27,28]	Upper gastrointestinal infection and symptoms of gastritis. Rates are higher in developing nations and in tropics
Tropical intestinal diarrhea syndromes with bacterial etiology			
Tropical sprue		Latin America, Southeast Asia, Caribbean[29]	Intestinal malabsorption of putative bacterial etiology (aerobic enteric gram-negative bacteria). Improvement with tetracyclines and folate supplementation. Probably similar to postinfectious irritable bowel syndrome
Whipple disease (*Tropheryma whipplei*)		Sub-Saharan Africa[30]	Chronic multisystemic infection with diarrhea in approximately 76% of patients. Disease uncommon in tropics but this may be due to underdiagnosis

Abbreviations: EAEC, enteroaggregative *E coli*; EHEC, enterohemorrhagic *E coli*; EIEC, enteroinvasive *E coli*; EPEC, enteropathogenic *E coli*; ETEC, enterotoxigenic *E coli*.

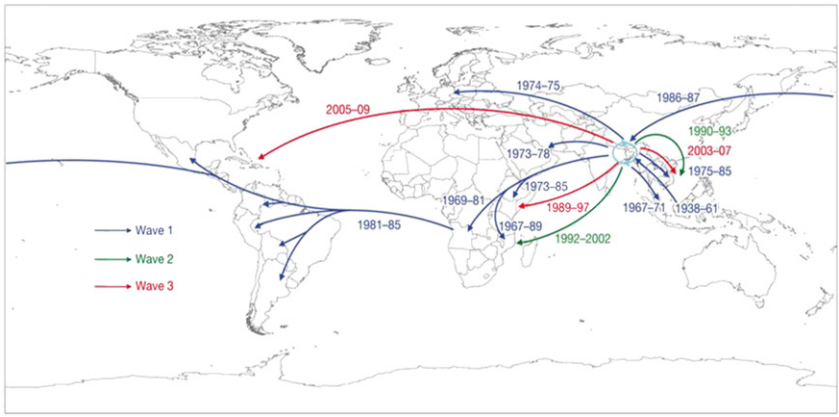

Fig. 2. Transmission events for the seventh *Vibrio cholerae* biotype El Tor pandemic. The information presented is inferred from phylogenetic reconstruction using single nucleotide polymorphisms (SNPs). Data generated by evolutionary parameter estimations in the Bayesian phylogenetic analysis software BEAST suggests the strains spread in 3 independent waves originating in the Bay of Bengal. (*Reproduced from* Mutreja A, Kim DW, Thomson NR, et al. Evidence for several waves of global transmission in the seventh cholera pandemic. Nature 2011;477(7365):464; with permission.)

The limitation for tropical regions in terms of culture, however, is availability, cost-effectiveness, and maintenance of laboratories with culture facilities and procedures.[47] Although National Reference Laboratories (NRLs) exist in WHO regions (tiered laboratory networks), their inaccessibility prevents timely diagnosis of bacterial infections.

Box 1
Clinical features in specific tropical bacterial gastrointestinal infections

Infection	Clinical Features
Diarrheal illnesses	
Cholera	Acute watery diarrhea ("rice-water"). High risk for rapid development of dehydration and death
Shigellosis	Severe diarrhea ± fever; often dysenteric. High risk of person to person transmission
Nontyphoidal salmonelloses	Acute self-limiting watery diarrhea; only occasionally with fever and dysentery. Zoonotic, foodborne (poultry, eggs, milk products)
Campylobacteriosis	Acute watery diarrhea, severe abdominal pain; often with fever and dysentery. Zoonotic, foodborne (poultry)
ETEC infection	Acute watery traveler's diarrhea; often self-limiting
EPEC/DAEC/EAEC infection	Acute watery diarrhea in infants and toddlers
Enteric fever	
Salmonella Typhi (commonest), followed by *Salmonella* Paratyphi A	Systemic illness; high-grade fever with diarrhea in children and constipation in adults as a rule
Salmonella Paratyphi B and *Salmonella* Paratyphi C are uncommon	High rate of life-threatening complications such as ileal perforations and chronic illness if untreated or inadequately treated

Because the yield of stool cultures for bacterial pathogens remains low,[46] screening tests may be useful in identifying specimens likely to give positive culture results. A summary of screening tests, their principle, sensitivity, and specificity are provided in **Table 2**. Algorithms using both screening and specific testing such as stool culture have been suggested. However, such combination is likely to incur additional costs for outreach health care systems in resource-poor tropical regions. It may therefore be more economical to skip screening tests in favor of specific prevalence-directed pathogen testing in endemic areas.

The unmet need for laboratory capacity building has affected prevalence statistics and availability of surveillance data. Once regional prevalence of pathogens is established, condensed diagnostic algorithms for targeted testing can be introduced in endemic areas, including dipstick testing for *S flexneri* 2a and *V cholerae.*[49,50] Individualized region-specific tiered laboratory systems may be developed whereby first-line testing can be performed using point-of-care (POC) dipstick tests, with confirmatory including culture-based testing being performed in the NRLs.[51]

Nucleic Acid Amplification Tests

Nucleic acid amplification tests (NAAT) have emerged as a sensitive, albeit relatively nonspecific alternative to stool cultures for rapid detection of pathogens from diarrheal stools.[52] Furthermore, microfluidic (dipstick) technologies integrated with NAAT, such as in laboratory chips or in laboratory-on-card systems, are in development; these methods will prove invaluable as low-cost, POC diagnostics of enteric infections in resource-poor tropical regions.[53]

Blood Cultures and Serology

Where invasive infections are suspected, a blood sample must be collected.[54] Blood and bone marrow cultures are the gold standards for detection of systemic salmonellosis. However, blood-culture sensitivity is affected by the number of organisms in the blood (being highest in the first week of illness) and by the volume of blood taken. Prior

Table 2
Summary of screening tests for acute infectious diarrhea

Test	Principle	Sensitivity	Specificity	Comments
Microscopy for fecal leukocytes	Identification of polymorphonuclear cells in stool (iodine, methylene blue stains)	73%	84%	Support diagnosis of inflammatory diarrhea.[45] Absent in noninflammatory enteritides such as cholera
Fecal lactoferrin	Iron-binding glycoprotein found in polymorphonuclear leukocytes	95%	29%	Support diagnosis of inflammatory diarrhea.[45,48] May miss noninflammatory and invasive etiology including *Vibrio cholerae* and ETEC
Fecal calprotectin	Protein released by leukocytes and macrophages in response to intestinal inflammation	—	—	Investigational; Initially developed as a test for inflammatory bowel disease. Potential marker for infectious diarrhea[2]

antibiotic therapy and type of culture media used also affect blood-culture sensitivity.[55] Serologic techniques may prove helpful in blood-culture–negative cases.[56] **Box 2** presents a list of some of the serologic tests based on antibody detection commonly available for diagnosis of enteric fever in the tropics.[37,55,57]

Sensitivity of serologic tests improve when paired sera are tested and with increasing duration of illness. Although in comparison to resource-intensive blood cultures serologic tests are more suitable as POC tests, further development using novel target antigens is warranted to increase their sensitivity.[58] To summarize, a broad range of diagnostic tests are available that need to be directed to imminent needs of tropical regions in relation to the prevalent pathogens.

PATHOPHYSIOLOGY AND PATHOGENESIS

Diarrhea is primarily a consequence of changes in electrolyte and fluid transport during passage through small and/or large intestines.[2] Pathogenesis of acute diarrhea is related to production of bacterial enterotoxins, and invasive and systemic pathogens adopt complicated mechanisms to induce disease.[2] **Table 3** lists pathogenic mechanisms of acute infectious diarrheagenic pathogens. Invasive *E coli*, Shigellae, and Salmonellae elaborate complicated molecular systems to attack enterocytes.[2]

Pathogenesis of enteric fever and molecular apparatus involved has only recently been elucidated. An excellent review by Andrews-Polymenis and colleagues[62] describes how current research has laid down basic mechanisms of disease in enteric

Box 2
Serologic tests for enteric fever

Test	Sensitivity (%)	Specificity (%)	Comments
Widal: Measures agglutinating antibodies against *Salmonella* Typhi lipopolysaccharide (LPS;O) and flagellar (H) antigens	64	76	Optimally requires testing of paired sera. Widal does not detect *Salmonella* Paratyphi A or Paratyphi B. Cross-reactivity with nontyphoidal Salmonellae and other Enterobacteriaceae is reported
Typhidot: Immunoblot method for specific immunoglobulin (Ig)M and IgG to 50-kDa *Salmonella* Typhi outer membrane protein	67–98	89–100	A qualitative assay. Its modified version; Typhidot M, detects immunoglobulin M as a more specific marker of acute infection Typhidot does not detect *Salmonella* Paratyphi A or Paratyphi B
TUBEX: Detects IgM to *Salmonella* Typhi O9 LPS through its ability to inhibit reaction between 2 colored antigen/antibody coated reagents	56–100	58–100	A 10-min semiquantitative assay that produces a visual readout. Newer versions of the test also detects *Salmonella* Paratyphi A[57]

Typhidot (Malaysian Biodiagnostics Research SDN BHD, Kuala Lumpur, Malaysia). TUBEX (IDL Biotech, Sollentuna, Sweden).

Table 3
Pathogenic mechanisms associated with diarrheagenic pathogens

Pathogen	Location of Pathology	Incubation	Infectious Dose	Toxin	Mechanism of Action
Vibrio cholerae	Proximal small bowel	12–72 h	10^2–10^6 organisms	Cholera toxin (CT)	Increased levels of cAMP[59]
Shigella spp	Colon	12 h	10^2–10^3 organisms	Shiga toxin (*Shigella dysenteriae* Type 1)	Single-site depurination of 28S ribosomal RNA causes inhibition of protein synthesis and cell death[60]
				Shigella enterotoxin 1 & 2 (ShET 1 & 2) in *Shigella flexneri* 2a	Induces fluid accumulation in rabbit ileal loops[60]
NTS	Colon	6–72 h	200–10^6 organisms	*Salmonella* enterotoxin (Stn); putative role	Immunologic relatedness to CT; cAMP-mediated secretory response in rabbit ileal loops
					Salmonella Pathogenicity Island (SPI)-encoded other factors, eg, T3SS[60]
E coli	—	2–4 d	—	—	—
EHEC	Colon	—	—	Shiga-like toxin	Similar to Shiga toxin[60,61]
EIEC	Colon	—	10^6 cells	—	Invasion of enterocytes through invasion-facilitating outer membrane proteins[60,61]
ETEC	Proximal small bowel	—	10^8 cells	Stable toxin (ST) Labile toxin (LT)	Increased levels of cGMP Similar to cholera toxin[60,61]
EPEC	Small bowel	—	10^6 cells	Putative new enterotoxin; EspB (EaeB)	3-Step model (adherence, signaling, and intimate adherence)[60,61]
EAEC	Small bowel	—	—	EAEC heat-stable enterotoxin (EAST 1), several others	Aggregative adhesive fimbriae, formation of biofilm on enteric epithelium[60,61]
Campylobacter	Colon	1–7 d	500–10^4 organisms	LT-like toxin	Increase in cAMP Microtubule-dependent invasion, disruption of cells[60]

Abbreviations: cAMP, cyclic adenosine monophosphate; cGMP, cyclic guanosine monophosphate; EAEC, enteroaggregative *E coli*; EHEC, enterohemorrhagic *E coli*; EIEC, enteroinvasive *E coli*; EPEC, enteropathogenic *E coli*; ETEC, enterotoxigenic *E coli*; NTS, Nontyphoidal salmonellae; T3SS, Type 3 secretion system.

fever. Although *Salmonella* Typhi shares basic pathogenic mechanisms with *Salmonella typhimurium*, a prolonged incubation period (average of 12 days), systemic infection, and gradual development of an inflammatory response in *Salmonella* Typhi infections suggests evasion of host immune defenses to a more sophisticated level. A likely responsible factor is the presence of genes encoding the Vi capsular polysaccharide; however, because this is absent in agents of paratyphoid fever, additional, as yet undiscovered, mechanisms may also exist.

MANAGEMENT

Management of Infectious Diarrhea

The cornerstone of management of acute infectious diarrhea is fluid replacement.[45] Oral rehydration and nutritional therapy (ORNT) regimens proposed by the WHO[63] are commonly used in the tropics. Although refractory vomiting and inability to take fluids orally may prompt parenteral fluid replacement, ORNT is more cost-effective, less invasive, and prevents against overhydration.[46]

The WHO recommends 20 mg of zinc daily for 14 days as a nonantimicrobial adjuvant to ORNT.[63] Zinc blocks basolateral potassium channels and inhibits chloride secretion.[2] Supplementation reduces severity and duration of illness in children.

Antibiotics are recommended for shigellosis and cholera, but not for other forms of acute watery diarrhea.[63] A recent survey of physicians advising travelers with diarrhea in the tropics found a high rate of polypharmacy, and empiric antibiotic usage (61%–95%).[64] While empiric antibiotic usage may be justified in areas with high prevalence of shigellosis and cholera, these areas also have a high rate of self-limiting salmonellosis and campylobacteriosis. Using antibiotics in such situations risks increasing antimicrobial resistance, antibiotic-associated diarrhea, and prolongs pathogen excretion in feces.[46]

Knowledge of current patterns of antimicrobial resistance is useful in establishing antibiotic policies and guidelines. Recent antimicrobial resistance trends of enteric pathogens in the tropics are presented in **Table 4**. However, generalizations regarding prevalence of antimicrobial resistance are difficult because resistance rates vary greatly geographically as well as temporally. NTS and typhoidal Salmonellae, for example, may regress to drug-sensitive phenotypes. Between the periods 1990-1999 and 2000-2004, sensitivity to ampicillin and cotrimoxazole increased in *Salmonella enteritidis* strains from Kenya.[70] Similarly, in India, susceptibility to first-line drugs ampicillin, cotrimoxazole, and chloramphenicol is reemerging in *Salmonella* Typhi strains.[79]

The resistance problem in turn begs the question of whether organism-based diagnostic including antimicrobial sensitivity testing is performed routinely. Indeed, if rapid POC microfluidic tests are widely available in underserved tropical regions, empiric antimicrobials will no longer be administered; hence the cavernous relationship of diagnostic tests to management and, unsurprisingly, to preventive measures.

Management of Enteric Fever: The Fluoroquinolone Resistance Perspective

Enteric fever was routinely treated in the 1960s with chloramphenicol, ampicillin, or cotrimoxazole. Emergence of multidrug-resistant (MDR) strains of typhoidal Salmonellae led to increasing usage of fluoroquinolones. Rapid emergence of fluoroquinolone nonsusceptible strains was soon reported.[79] Nowadays in most areas including the Indian subcontinent, ceftriaxone and cefixime remain the only reliable antimicrobial choices.[36] A summary of empiric treatment of bacterial gastrointestinal infections is given in **Box 3**.

Table 4
Antimicrobial resistance trends of enteric pathogens in the tropics

Pathogen	Tropical Regions	Recent Antibiotic Resistance Rates (%) and Trends
Vibrio cholerae	Africa	Kenya (1999): multiple drug resistance to C, SXT, TE[65]
		Angola (2006): multiple resistance to AMP, C, SXT, TE[66]
	Asia	Iraq: resistant to SXT[10]
		India (2010): multiple resistance to AMP, NA, SXT, C, TE (>70%)[12]
	Latin America	Brazil (1999): AMP, SXT, furazolidone (70%–80%)[67]
Shigella spp	Africa	Tanzania (1999): AMP, C, SXT, TE (>70%)[68]
		Kenya: SXT, TE, AMP (95%–100%)[69]
	Asia	Iran: AMP, SXT, TE (100%)[17]
		Taiwan: NA, SXT (100%)[18]
	Latin America	Brazil: AMP, SXT (>80%). Variable resistance to TE, C[16]
NTS	Africa	*S enteritidis*; AMP, SXT (>90%) in 1999, decreasing trend (2004) *S typhimurium*; AMP, SXT (>90%) (1999–2004)[70]
	Asia	India (2002): AMP (60%), NA (66%), FQ (18%), SXT (34%), C (37%), 3GC (48%)[71]
	Latin America	Mexico: multidrug resistance in *S typhimurium* increased from 0% to 75% (2000–2005)[72]
DEC	Africa	Kenya: resistance rates; AMP (65%), SXT (68%), TE:70%[73]
	Asia	India (2006): AMP (85%), SXT (64%), NA (85%), FQ (79%)[74]
	Latin America	Brazil (2007): SXT (35%), multidrug resistance (3%–5%)[75]
Campylobacter	Africa	Uganda (2005): AMP (20%), FQ (5%), 100% susceptible to E[76]
	Asia	Indonesia (2001): AMP (65%), SXT (70%), TE (65%), FQ (45%), 100% susceptible to E[77]
Typhoidal Salmonellae (TS)	Africa	2002–2008: MDRTS (29%–70%) geographic prevalence variation[78]
	Asia	1992–2005: MDRTS (1.3%–80%) geographic prevalence variation[78]

Abbreviations: AMP, ampicillin, 3GC, third-generation cephalosporins; C, chloramphenicol; DEC, diarrheagenic *E coli*; E, erythromycin; FQ, fluoroquinolones; MDRTS (multidrug-resistant TS), resistant to AMP, SXT, C; NA, nalidixic acid; SXT, cotrimoxazole; TE, tetracycline.

PREVENTION

Most authorities recommend exercising care in selecting food and beverages to prevent diarrhea. In resource-limited tropical regions, however, inculcating this tenet is a challenge. Additional measures on a public scale are required: improving sanitation and sewage disposal and drainage, provision of safe drinking water, and widespread vaccination to generate herd immunity where applicable.[46]

Enteric Vaccines

The WHO prioritizes vaccination against agents causing high morbidity and mortality, especially among children in underdeveloped nations.[2] A summary of the available vaccines for bacterial gastrointestinal infections is given in **Box 4**.

Box 3
Recommended agents for treatment of bacterial gastrointestinal infections

Pathogen	Recommended Agents
Vibrio cholerae	Antibiotics not essential. Oral doxycycline (300 mg single dose in nonpregnant adults), oral azithromycin (1 gram single dose in pregnant females; 20 mg/kg in children as a single dose) decreases symptomatic illness and fecal shedding
Shigella spp	Quinolones (ciprofloxacin 500 mg orally twice daily in adults or 10 mg/kg twice daily in children) or cotrimoxazole (160/800 mg twice daily in adults and 5/25 mg/kg twice daily in children) for 3–5 days
Salmonella enteritidis and other NTS	Antibiotics not indicated in otherwise healthy individuals, as may prolong illness and fecal shedding. Immunocompromised and debilitated patients may be treated according to susceptibility results.
Campylobacter spp	Quinolones (500 mg ciprofloxacin twice daily) or erythromycin (500 mg 4 times daily) for 5 days, although usually self-limiting. For children, erythromycin is preferable to quinolones (dosage for erythromycin: 10 mg/kg orally 4 times daily for 5 days)
Diarrheagenic *E coli*	Quinolones (ciprofloxacin 500 mg orally twice daily) or cotrimoxazole (160/800 mg twice daily) for 2–5 days for ETEC, EPEC, EIEC, and DAEC. Dosages for children for severe EPEC and EIEC, or DAEC disease are cotrimoxazole at 5 mg trimethoprim/kg body weight for 3 days. Quinolones should be avoided in children. Caution is required in EHEC-induced postinfectious hemolytic uremic syndrome for which antibiotics are contraindicated
Enteric fever	
Salmonella Typhi, *Salmonella* Paratyphi A (*Salmonella* Paratyphi B and *S* Paratyphi C uncommon)	Treatment of uncomplicated cases with oral cefixime 30 mg/kg/d divided 12-hourly or azithromycin 10 mg/kg/d for 7 days (both children and adults); complicated cases require initial parenteral ceftriaxone 60–80 mg/kg/d divided 12-hourly or cefotaxime 100–150 mg/kg/d divided 8-hourly (both children and adults) followed by oral antibiotics to complete 10–14 days

Vaccines available for cholera include Dukoral, Shanchol, and mORCVAX. The current WHO position is to use these vaccines in areas at risk of outbreaks, and in high-risk populations in endemic areas.[80] Because of the lack of data it is difficult to comment on coverage of these vaccines in target populations.

Commercially available *Salmonella* Typhi vaccines include Ty21a and Vi polysaccharide vaccine. Ty21a provides a 53% to 78% 3- to 7-year protection after 3 doses, whereas Vi polysaccharide vaccine provides 70% protection after 1 dose for 3 years.[81] The WHO recommends routine programmatic vaccination of high-risk populations in endemic countries.[81] Recent field trials of programmatic vaccination in India, Egypt, and Chile have demonstrated good results.[82]

Vaccines against *Shigella* spp and ETEC are less forthcoming, owing to a multitude of serotypes causing infections.[2] A new generation of unlicensed vaccines against these pathogens is currently undergoing clinical trials.[2]

Box 4
Licensed vaccines for bacterial gastrointestinal infections

Vibrio cholerae vaccines

- Inactivated whole cell (serogroup 01) + cholera toxin B-subunit vaccine (Dukoral): oral vaccine for children and adults; 2 doses
- Inactivated Bivalent (O1 and O139) oral cholera vaccines (Shanchol and mORCVAX): recommended for children older than 1 year and adults; 2 doses 2 weeks apart

Salmonella Typhi vaccines

- Ty21a: oral vaccine for children older than 2 years and adults; 3 doses 48 hours apart
- Vi polysaccharide: parenteral vaccine for children older than 2 years and adults; single dose

SUMMARY

The tropics are endemic for several bacterial gastrointestinal infections. Globalization and widespread travel have led to geographic boundaries becoming increasingly indistinct as markers of disease occurrence. One must, therefore, consider the occurrence of tropical diseases outside of the tropics. Within the latitudinal limits of the tropics, recent surveillance data is essential to inform diagnostic measures, management, and preventive strategies. Financial and human resource constraints continue to hinder effective implementation of such surveillance measures. However, recent initiatives by nongovernmental funding resources toward generating such data[31] are a welcome change, and may lead to individualized guidelines for gastrointestinal illness in the tropics.

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