Food and water-borne illness

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- Vaccines
  - Hepatitis A
  - Typhoid
  - Cholera
  - (not Rotavirus, polio)

- Travellers' Diarrhea

Estimated VPD incidence

Logarithmic scale

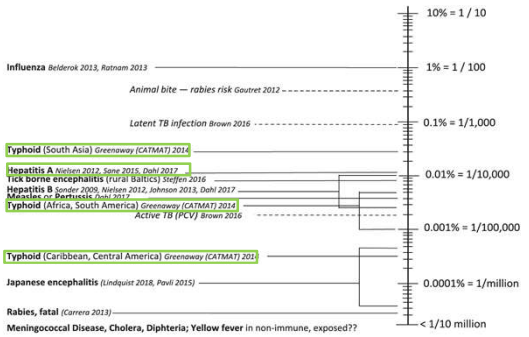
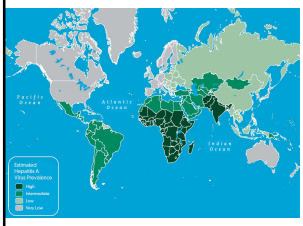


Figure 1. Vaccine preventable disease travel health risks: Estimated incidence per month in lower income countries among non-immunes

Steffen, R. 2018 J Travel Med https://doi.org/10.1093/jtm/tay046

Hepatitis A



Map, CDC Travel site: https://wwwnc.cdc.gov/travel/images/map3-3-estimated-prevalence-hepatitis-a-large.png

- Faecal-oral transmission
  - Contaminated water and food
  - Direct person-to-person contact
- Risks for infection
  - Travellers, MSM, occupational (e.g. childcare, sewage workers)
- Recent traveller incidence estimate ~1 (0.6-2.8) in 10,000 per month
  - Global incidence reducing
  - Still an important vaccine-preventable travel infection

Hepatitis A infection

- HAV characteristics
  - Shed in faeces for 1-2 weeks before symptom onset, ~6 weeks to 6 months post infection
  - Prolonged environmental HAV survival
    - Inactivated at high temps, not by freezing
- Clinical
  - Asymptomatic -> severe disease
    - Influenced by age: 70% of <6yo asymptomatic
  - Overall case-fatality rate = 0.3% (>50 yrs = 1.8%)
  - Rare severe complications (fulminant hepatitis, liver failure)
- Chronic infection does not occur, life-long immunity after infection

https://wwwnc.cdc.gov/travel/yellowbook/2020/travel-related-infectious-diseases/hepatitis-a

Hepatitis A vaccines

Monovalent hepatitis A vaccines

- *Avaxim* – Sanofi-Aventis, 160 antigen units of inactivated HAV, >=2 yo, 0.5mL
- *Havrix Junior* – GSK, 720 ELISA units of inactivated HAV, 2-<16 yo*, 0.5mL
- *Havrix 1440* – GSK, 1440 ELISA units of inactivated HAV, >=16 yo*, 1mL
- *Vaqta Paediatric/Adolescent formulation* – Merck Sharp & Dohme, 25 units (U) of HAV protein, 1-<18 yo, 0.5mL
- *Vaqta Adult formulation* – Merck Sharp & Dohme, 50U of HAV protein, >=18 yo, 1mL

Combination vaccines including hepatitis A

- *Twinrix Junior (360/10)* – GSK, 360 ELISA units of HAV antigens, 10 µg recombinant DNA hepatitis B surface antigen protein, 1-<16 yo *, 0.5mL
- *Twinrix (720/20)* – GSK, 720 ELISA units of HAV antigens, 20 µg recombinant DNA hepatitis B surface antigen protein, >=16 yo*, 1mL
- *Vivaxim* – Sanofi-Aventis, 160 antigen units of inactivated HAV, 25 µg purified typhoid Vi capsular polysaccharide, >=16 yo, 1mL

*US CDC: >18 yo

https://immunisationhandbook.health.gov.au/contents/vaccine-preventable-diseases/hepatitis-a#vaccine-information

Hepatitis A vaccine

- Recommended for people ≥1 year of age travelling to moderately or highly endemic countries
- Highly immunogenic in healthy children and adults
  - Single vaccine dose provides protective Ab levels for at least 1 year
- 2nd dose at 6 - 12 months increases duration of protection
  - Seroconversion nearly universal 4 weeks after vaccination
  - No difference in immunogenicity with standard (6-12 months) vs. extended (20-31 months) dose intervals
  - No evidence boosters are required in healthy individuals
- Serological testing not routinely recommended pre-vaccination unless born before 1950, childhood in endemic areas, Hx of unexplained hepatitis

https://immunisationhandbook.health.gov.au/contents/vaccine-preventable-diseases/hepatitis-a#vaccine-information

Hepatitis A vaccine in immunocompromised

- Single dose may not afford sufficient protection and durability of response is uncertain
- Approach depends on risk, timing of travel, vaccination/ exposure history & serology
  - Perform serology if previously vaccinated*
  - Active immunisation approach: consider extra dose (double dose or 1 month booster), perform serology to check for seroconversion*
  - Passive immunisation approach: Hepatitis A immunoglobulin but difficult to source & may provide limited protection given low overall seroprevalence

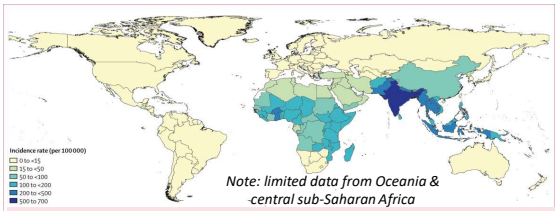
*Antibody titres following vaccination may be below detection limits of commercial tests

Typhoid (*Salmonella* Typhi)

- Case of Enteric fever (along with Paratyphi)
- Transmission
  - Contaminated food and water
  - Person-to-person
- Travellers at most risk
  - VFRs, backpackers, trips >1 month
- Highest risk destinations
  - South Asia (1 in 5000 per month of stay) then Sth America & Africa (approx 10-fold lower risk)
- ~5% of those who recover without treatment will become chronic carriers (asymptomatic & infectious)

Enteric fever (Typhoid & Paratyphoid)

Figure: incidence rates (per 100,000) of typhoid and paratyphoid fevers, by country (2017)



	Cases (thousands)		
	Typhoid fever	Paratyphoid fever	Percentage typhoid fever
Global	10 924·3 (9343·0–12 597·1)	3396·9 (2666·5–4184·1)	76·3% (71·8–80·5)

GBD 2017 Typhoid and Paratyphoid Collaborators. *Lancet Infect Dis.* 2019; 19
https://doi.org/10.1016/S1473-3099(18)30685-6

Typhoid vaccines

Monovalent typhoid vaccines

•*Vivotif Oral* – CSL Limited/Crucell Switzerland AG. Oral live attenuated typhoid vaccine containing viable attenuated *S.* Typhi strain Ty21a, 3 capsules in blister pack, >=6 yrs

•*Typherix* – GlaxoSmithKline, purified Vi capsular polysaccharide vaccine, >=2 yrs

•*Typhim Vi* – Sanofi Pasteur Vi polysaccharide of *S.* Typhi strain Ty2, >=2 yrs

Conjugate vaccines

Typbar-TCV – Bharat Biotech, >6 months
PedaTyph – BioMed, >3months

Combination vaccine

•*Vivaxim* – Sanofi Pasteur Pty Ltd (inactivated hepatitis A virus and typhoid Vi capsular polysaccharide), >=16 yrs*

* Combined hepatitis A/typhoid vaccine licensed ≥16 years, but can be given down to 2 years

Typhoid vaccine - travellers

- Those aged ≥2 years are recommended to receive **typhoid vaccine** if travelling to endemic regions:
  - Where food hygiene may be suboptimal and drinking water may not be properly treated, and/or
  - To visit friends and relatives (VFRs)
- Travel to areas where strains partially or completely resistant to many antibiotics (including ciprofloxacin) are common
  - Esp Indian subcontinent

https://immunisationhandbook.health.gov.au/vaccine-preventable-diseases/typhoid-fever
NNDSS Annual Report Working Group. *CDI.* 2019; 43

Cholera

Cholera vaccines

- Oral inactivated
  - ShanChol, Euvichol-Plus, mORCVaxX – same vaccine, different manufacturers
    - Licensed from 1 year
    - 2 doses at least 2 weeks apart provide 3 year-protection
    - Do protect against O139 strain
    - Used in mass vaccine campaigns
- Vaxchora
  - Approved in US for adults 18-64 yo
  - Live, oral
  - Efficacy – 80-90% for up to 3 months

Cholera vaccines

- Dukoral –inactivated whole-cell *V. cholerae* O1, combined with recombinant cholera toxin B subunit [rCTB]
  - Oral but inactivated
  - Efficacy: 60-80% against cholera but varies with age
  - Does not protect against the *V. cholerae* O139 serogroup
- Children aged 2–6 years: 3 doses, 1 to 6 weeks apart, boost at 6 months
- >6 years: 2 doses, 1 to 6 weeks apart, boost at 2 years
- Cholera and ETEC share same toxin: cholera vaccine gives some partial short-term (3 months) protection against ETEC TD (approx 50% ↓ in ETEC, overall reduces TD by ~ 10-20%)

Travellers' diarrhoea

Table 1 Etiologies of travelers' diarrhea

Agent[a]	Frequency (%)[b]
Bacteria	50–75
Escherichia coli (enterotoxigenic)	10–45
E. coli (enteroaggregative)	5–35
Campylobacter spp.	5–25
Salmonella spp.	0–15
Shigella spp.	0–15
Bacteriodes fragilis (enterotoxigenic)	0–10
Others[c]	0–5
Viruses	5–20
Noroviruses	0–10
Rotavirus	0–5
Parasites	0–10
Giardia intestinalis	0–5
Cryptosporidium spp.	0–5
Cyclospora cayetanensis	<1
Entamoeba histolytica	<1
Acute food poisoning	0–5
No pathogen identified	10–50

Bacteria

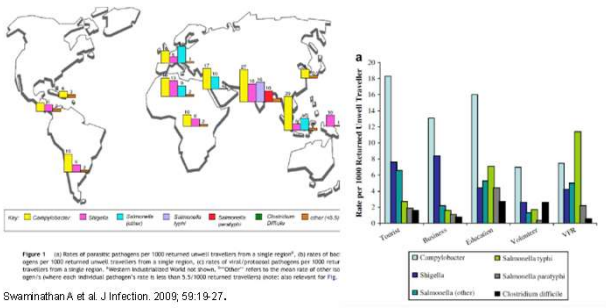
Viruses

Parasites

- New diagnostics -> multipathogens common

Hill DR et al. *Curr Opin Infect Dis* 2010; 23(5):481-7

Variation in aetiology by region & travel purpose



Swaminathan A et al. J Infection. 2009; 59:19-27.

Travellers' diarrhea General advice

Food

- All raw food is high risk
  - Avoid salads, uncooked vegetables, unpasteurized milk and cheese
  - Eat food that has been cooked and is still hot or fruit that can be peeled
  - Undercooked and raw meat, fish, and shellfish are high risk
- Avoid food from street vendors

Water

- If chlorinated tap water is unavailable or sanitation is poor, only the following are safe to drink:
  - Beverages made with boiled water
  - Canned or bottled beverages
  - Beer and wine
- Avoid ice and avoid brushing teeth with tap water

Travellers' diarrhoea

Poor efficacy of food and water precautions
- Where you eat, more important than what you eat

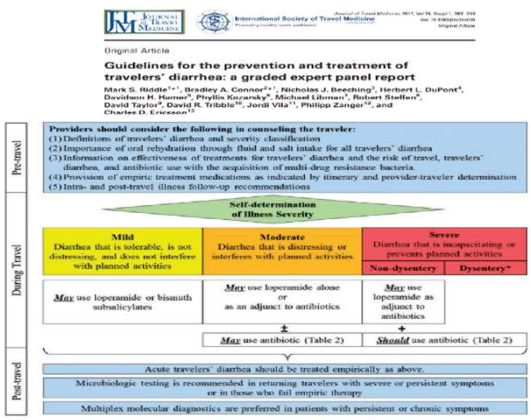
TD

- Natural history
  - Usually resolves in 1-2 days
  - 10% cases last >1 wk
  - 2% last >1 month
  - <1% last >3 months
- Self-Rx options: hydration PLUS
  - Watch and wait
  - Antimotility agents for symptomatic relief
    - Loperamide (imodium, gastrostop): 2 capsules stat, then 1 after each loose bowel motion, max 8 tabs per 24 hours
  - Antibiotics or combination antimotility/antibiotics
    - Don't use loperamide alone for TD if temp>38.5C or bloody stools

Antibiotics

- Azithromycin
  - 500 mg per day for 1–3 days
  - Start: frequent, loose, fever, blood. Stop: when better
  - Resistance emerging (up to ¼ -⅓ of isolates from Asia)
- Rifaximin
  - 200 mg tabs tds x 3 days, licensed in US & many EU countries
  - Non absorbable antibiotic, not effective for invasive pathogens (eg *C. jejuni, Shigella)*
- Use of antibiotics for acute TD now controversial because of MDR and microbiome disruption, balance risks vs benefits
  - Gut microbiome changes occur in travellers with / without diarrhea, with / without loperamide, with / without antibiotics, but worse with antibiotics
  - Increasing association between travel, TD, and antibiotic use with acquisition of multidrug-resistant bacteria

https://doi.org/10.1093/jtm/tax026


Original Article

Guidelines for the prevention and treatment of travelers' diarrhea: a graded expert panel report

Mark S. Riddle[1,*], Bradley A. Connor[2,*], Nicholas J. Beeching[3], Herbert L. DuPont[4], Davidson H. Hamer[5], Phyllis Kozarsky[6], Michael Libman[7], Robert Steffen[8], David Taylor[9], David R. Tribble[10], Jordi Vila[11], Philipp Zanger[12], and Charles D. Ericsson[13]

Providers should consider the following in counseling the traveler:
(1) Definitions of travelers' diarrhea and severity classification
(2) Importance of oral rehydration through fluid and salt intake for all travelers' diarrhea
(3) Information on effectiveness of treatments for travelers' diarrhea and the risk of travel, travelers' diarrhea, and antibiotic use with the acquisition of multi-drug resistance bacteria
(4) Provision of empiric treatment medications as indicated by itinerary and provider-traveler determination
(5) Intra- and post-travel illness follow-up recommendations

Pre-travel

Self-determination of Illness Severity

During Travel

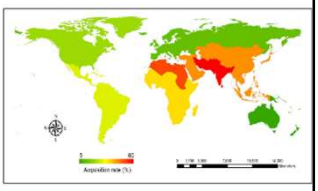
Mild	Moderate	Severe	
Diarrhea that is tolerable, is not distressing, and does not interfere with planned activities	Diarrhea that is distressing or interferes with planned activities	Diarrhea that is incapacitating or prevents planned activities	
		Non-dysentery	Dysentery*
May use loperamide or bismuth subsalicylates	*May* use loperamide alone or as an adjunct to antibiotics	*May* use loperamide as adjunct to antibiotics	
	May use antibiotic (Table 2)	*Should* use antibiotic (Table 2)	

Post-travel

Acute travelers' diarrhea should be treated empirically as above.
Microbiologic testing is recommended in returning travelers with severe or persistent symptoms or in those who fail empiric therapy
Multiplex molecular diagnostics are preferred in patients with persistent or chronic symptoms

Risk factors for AMR acquisition

- AMR acquisition in 30% travellers
- Risk factors
  - Destination (Asia >50-60%)
  - TD
  - Healthcare during travel
  - Antibiotics
  - Antibiotics plus loperamide
  - Inflammatory bowel disease
  - Diet (vegetarians)
  - Type of traveller - backpackers



Furuya-Kanamori L et al. *J Travel Med* 2020. https://doi.org/10.1093/jtm/taz083

Variable duration of carriage: can be prolonged (>6 months)

Bovine colostrum and pre/probiotics

- Bovine colostrum (Travelan®)
  - Need to take tablet before every meal
  - Protective efficacy: up to 90% against ETEC
  - Data regarding overall efficacy of reducing all-cause TD currently lacking
- Pre and probiotics
  - No evidence of benefit for use of commercially available prophylaxis or treatment of TD

Otto W et al. *Scand J Gastroenterol* 2011 https://doi.org/10.3109/00365521.2011.574726