A primer on travel-related infections

Seminar on travel-related infections and tropical diseases.

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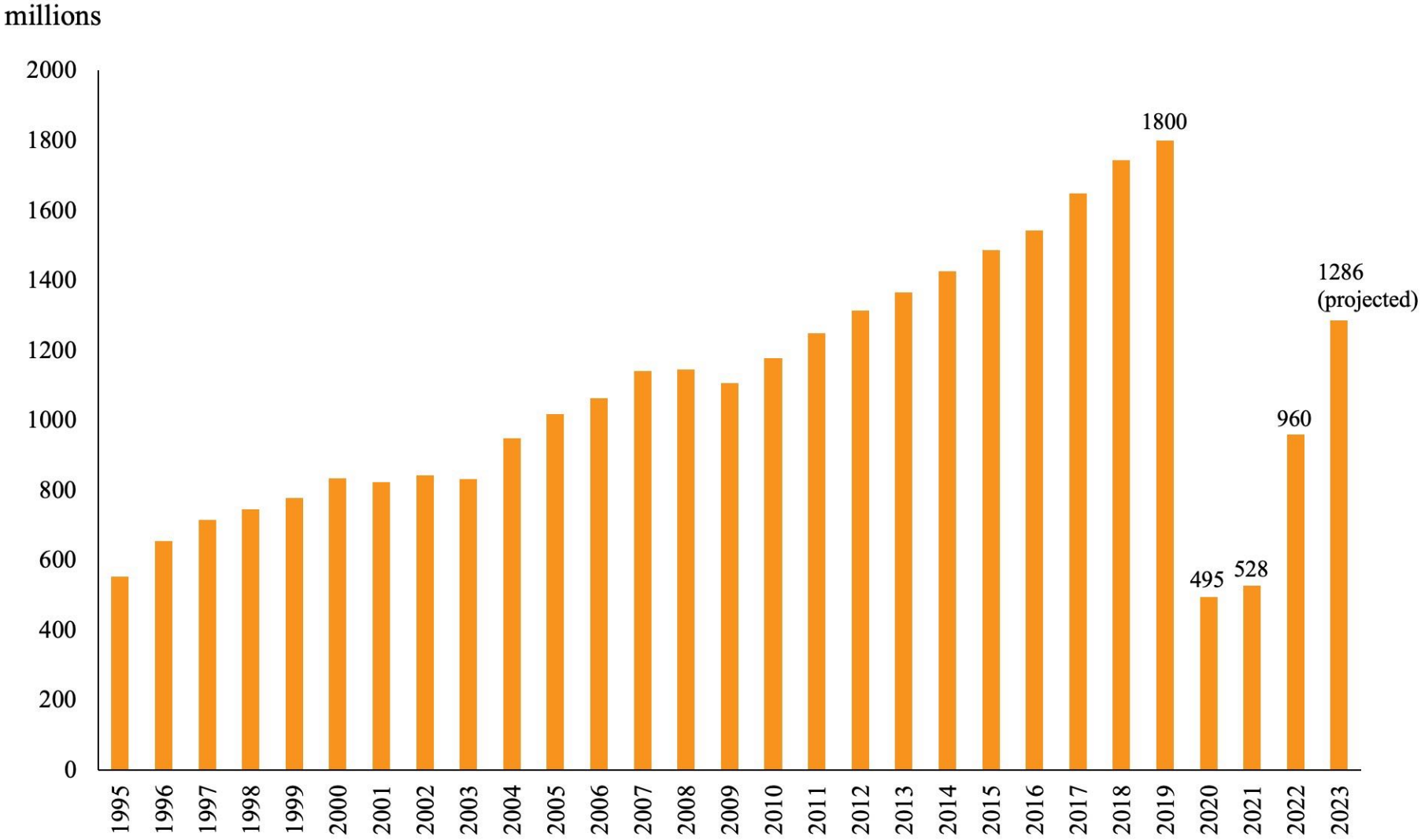
2/2/2024

International tourist arrivals



https://ourworldindata.org/tourism. Data source: United Nations World Tourism Organization (UNWTO, 2023)

Risk of travel-related infection or other illnesses

- Destination.
- Duration.
- Reason for travel (e.g. business, visiting friends and relatives).
- Season.
- Type of travel (e.g. backpacking, rural/urban).
- Behaviour of traveller.
- Prophylactic measures.
- Host factors.

Torresi J, McGuinness S, Leder K, O'Brien D, Ruff T, Starr M, Gibney K (ed). *Manual of Travel Medicine*, 4th edition, 2019.

Travel-related illnesses are not just infections.

Travel-related deaths

Table 3.8 Causes of death among tourists (different studies)

Cause of death	Hargarten *et al.* 1991 (n = 2463)	Steffen *et al.* 2003 (n = 247)	Steffen *et al.* 2003 (n = 68)	Provic *et al.* 1995 (n = 421)	Paixao *et al.* 1995 (n = 952)	McPherson *et al.* 2007 (n = 2410)
Origin destinations	US anywhere	Swiss Europe	Swiss overseas	Australia overseas	Scotland anywhere	Canada anywhere
Cardiovascular	**49%**	**14%**	**15%**	**35%**	**69%**	**52%**
Infection	1%	nd	3%	2%	4%	nd
Cancer	6%	nd	nd	nd	nd	nd
Injury/accident	**36%**	**23%**	**44%**	**54%**	**21%**	**19%**
– traffic	7%	13%	12%	28%	nd	nd
– air crash	2%	4%	12%	nd	nd	nd
– drowning	4%	4%	9%	nd	nd	nd
– other	23%	2%	11%	26%	nd	nd
Suicide/homicide	3%	nd	nd	8%	nd	8%
Other, unknown	19%	58%	29%	17%	7%	nd

- Cardiovascular diseases and accidents consistently the leading causes of death in travellers.
- Injury accounts for ~25% of deaths in travellers.

Nothdurft HD, Caumes E. Epidemiology of health risks and travel. In: Zuckerman JN (ed). *Principles and Practice of Travel Medicine*. Blackwell Publishing Ltd. 2013, p 19–26.
https://ourworldindata.org/grapher/death-rates-road-incidents?tab=chart
https://ourworldindata.org/grapher/number-of-deaths-from-road-injuries?tab=table
Wyler BA, Young HM, Hargarten SW, Cahill JD. Risk of deaths due to injuries in travellers: a systematic review. *J Travel Med* 2022;29:taac074.

Approach to travel-related infections

Difficulties

- Detailed travel history required.
- Knowledge in exotic diseases.
- Awareness of tropical diseases.
- Awareness of latest infectious disease outbreaks.

As of 14/1/2024

27,991 suspected cases of diphtheria, 828 fatalities.

Since 1/1/2022, 295,691 cases of cholera 5,421 deaths. Since 1/1/2024, 11,415 and 355 deaths.

History

- Detailed history of present illness.
  - Onset: incubation period.
  - Duration.
  - Symptomatology: local, systemic.
  - (Fever pattern)
- Underlying diseases and medications of the traveller.

Incubation periods

TABLE 1

Incubation periods of febrile travel-related infectious diseases in detail, adapted from (21, e5–e7)

Incubation period	Bacteria	Viruses	Parasites
<14 days	• **Anthrax**: 1–6 d • **Bacterial diarrhea:** – Campylobacteriosis: 1–10 d – Salmonellosis (NTS): 12–48 hrs – Shigellosis: 1–5 d – Cholera: few hrs – 5 d • **Legionellosis:** 5–6 d • **Leptospirosis:** 7–12 d • **Melioidosis** 2–21 d (rarely mths to yrs) • **Meningococcal meningitis/sepsis:** 2–10 d • **Plaque:** Bubonic plague: 2–6 d – Primary pneumonic plague: hrs to 2–3 d • **Rickettsioses** (spotted fever and tick-bite fever group, Tsutsugamushi fever): 2–14 d • **Relapsing fever:** 7 d (2–18 d) • **Typhoid fever:** 7–18 d • **Paratyphoid fever:** 1–10 d	• **Arboviral disease** (dengue fever, Chikungunya fever, Zika fever, yellow fever, Japanese encephalitis, Rift Valley fever, West Nile fever): 1–14 d • **Measles:** 10–14 d • **Rabies:** rarely <14 d • **Viral hemorrhagic fevers** (Ebola HF, Lassa HF, Marburg HF, Crimean–Congo HF, yellow fever): 2–21 d • **Viral diseases of the respiratory system:** Influenza: 1–3 d, SARS-CoV-2 infection/COVID-19: 5–6 d • **Viral gastroenteritis** (e.g., norovirus, rotavirus): 1–2 d	• **Malaria:** Plasmodium (P.) falciparum: 6–30 d, P. knowlesi: 10–14 d • **East African trypanosomiasis** (sleeping sickness): 7–21 d
14 days to 6 weeks	• **Bartonellosis:** 3 wks (2–14 mths) • **Brucellosis:** 1–3 wks (to several mths) • **Melioidosis:** 2–21 d (to several years) • **Q fever:** 2–3 wks • **Typhoid fever:** 7–18 d	• **Acute HIV infection:** 10–28 d • **Hepatitis A:** 15–50 d (usually 25–30 d) • **Hepatitis E:** 26–42 d • **Rubella:** 14–21 d • **Rabies:** 20–90 d	• **Malaria:** P. falciparum: 6–30 d, P. vivax/ovale: 12 d –12 Mo, P. malariae: 13–28 d • **Acute schistosomiasis** (Katayama fever): 28–60 d
>6 weeks	• **Tuberculosis:** 6–8 wks (primary infection), usually asymptomatic	• **Hepatitis B:** 60–150 d • **Rabies:** rarely up to years	• **Malaria:** P. vivax/ovale: up to 12 mths • **Amoebic liver abscess:** wks to mths • **Visceral leishmaniasis:** 2–10 mths • **West African trypanosomiasis:** wks to mths

d, days; HF, hemorrhagic fever; hrs, hours; mths, months; NTS, non-typhoidal Salmonella; wks, weeks

Paquet D, Jung L, Trawinski H, Wendt S, Lübbert C. Fever in the returning traveler. *Dtsch Arztebl Int* 2022;119:400–407.

History

- Complete travel history.
- Sexual exposure.
- Needle and blood exposure.
  - Drug abuse, tattoos, body piercing, injection, medical procedures, transfusion; medical tourism.
- Animal/arthropod contacts.
  - Bites, scratches, licks; spelunking.
- Exposure to water.
  - Swimming, walking, rafting.
- Food/drink exposure.
- Prophylactic measures.
  - Vaccines, chemoprophylaxis.
  - Compliance to chemoprophylaxis.

Table 15.1 Initial questions for the travel history

When

- When did you last travel outside the country? Exact dates of departure and return
- When did you last travel away from home? When did you travel before that?
- When did you first get ill? Exact dates if possible

Where

- Where were you born?
- Where exactly did you go on this trip? Precise location, not just country or continent
- Where did you stop along the way?

Why

- Why did you go abroad? Business, tourism, visiting family, etc.

What

- What health problems did you already have before travel?
- What method of transport did you use?
- What did you do there? Risk activities – freshwater contact, etc.
- What precautions did you take before you went? List immunisations, etc.
- What precautions did you take while there? Quantify adherence to safe eating, safe sex, antimosquito measures

Who

- Who else went with you?
- Who else got ill?

Beeching NJ, Fletcher TE, Wijaya L. Returned travellers. In: Zuckerman JN (ed). *Principles and Practice of Travel Medicine*, 2nd edition. Wiley-Blackwell. 2013.

Exposure history and infections

Exposure	Potential infective complications
Sex, blood, body fluids, intravenous drug use	Hepatitis B and C, HIV infection, syphilis, other sexually-transmitted infections/infestations, monkeypox/Mpox.
Tattoos, body piercing, other body modification procedures	Hepatitis B and C, HIV infection, syphilis, non-tuberculous mycobacterial infections.
Hospitalization, surgical procedures	Drug-resistant organisms (colonization or infection), bloodborne viruses.
Ingestion of raw or undercooked food	Various foodborne infections including bacterial and viral gastroenteritis, protozoal and helminth infections, brucellosis, listeriosis, toxoplasmosis, hepatitis A and E.
Soil	Histoplasmosis, coccidioidomycoses, other endemic mycoses, cutaneous larva migrans, strongyloidiasis; melioidosis.
Freshwater	Schistosomiasis (Katayama fever), leptospirosis, skin and soft tissue infections (*Aeromonas*, *Vibrio*), primary amebic meningoencephalitis; gastrointestinal infections; melioidosis.
Arthropod bites	Arthropod-borne infections, e.g. dengue, chikungunya, Zika virus infection, rickettsioses, relapsing fevers, malaria, babesiosis, leishmaniasis, trypanosomiasis, dirofilariasis.
Dog, bat and other animal bites	Rabies, bat rabies, herpes B virus infection, bite wound infections.
Animals and animal products	Hantaviruses, Lassa fever, Crimean-Congo haemorrhagic fevers, avian influenza, MERS, plague, rat-bite fevers, leptospirosis, Q fever, brucellosis, tularaemia, anthrax, psittacosis.

Physical examination

- General, e.g.
  - Skin (rash, eschar, bite marks, needle marks) and mucosal lesions.
  - Ocular signs.
  - Jaundice.
  - Haemorrhagic manifestations.
- Systemic, e.g.
  - Lymphadenopathy.
  - Organomegaly.
  - Other localizing signs.

Investigations

- Haematology.
  - Cell counts and differential; coagulation studies.
- Biochemistry.
- Imaging.
- Microbiological.
  - Microscopy.
    - Blood, stool, urine, sputum.
  - Culture.
    - Blood, stool, urine, other relevant specimens.
  - Serology.
  - Nucleic acid amplification.
    - Targeted; syndromic testing.
- Tissue biopsy.
  - Histopathology, microbiology.

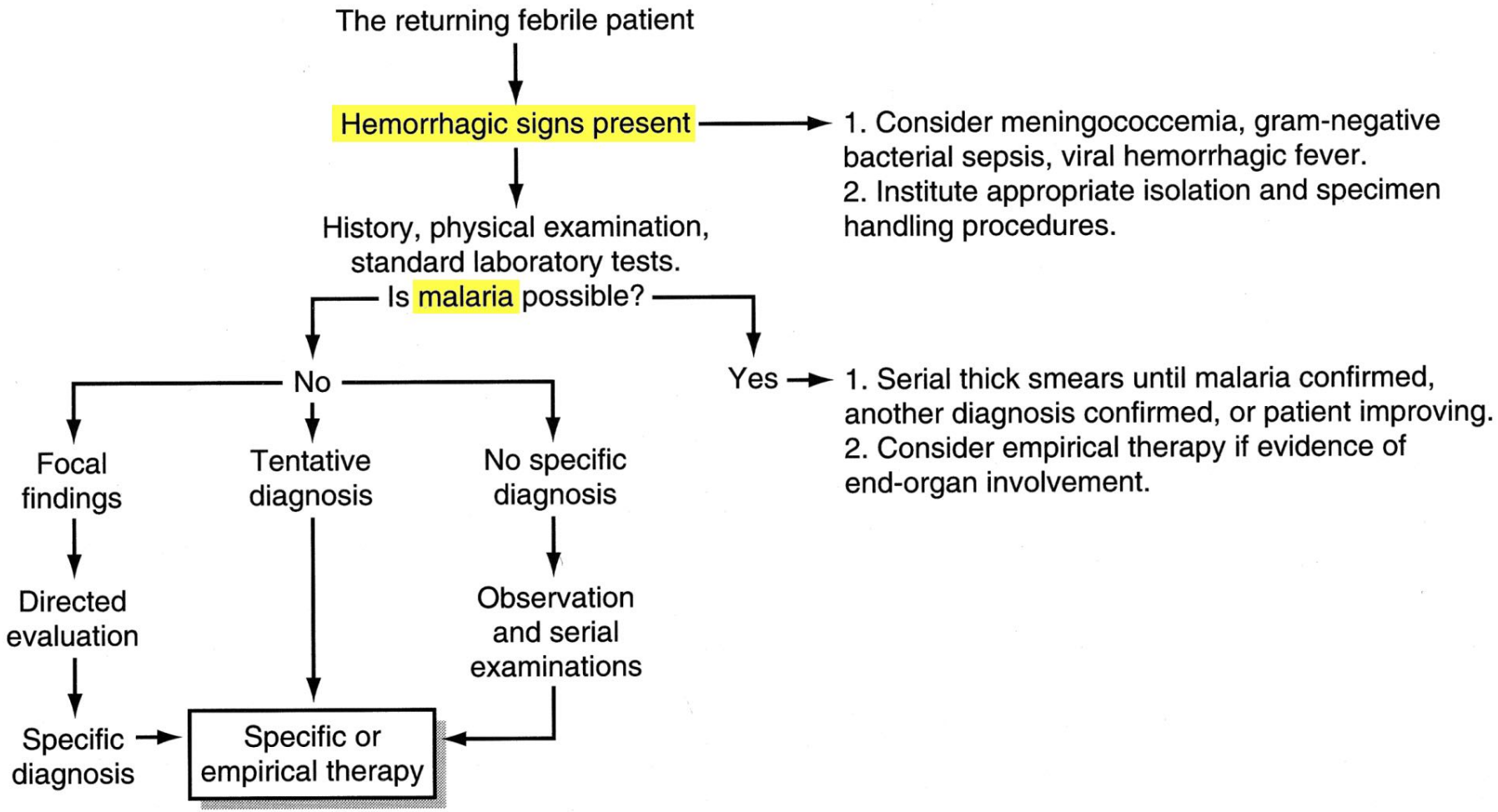
As appropriate

Presumptive (differential) diagnoses

- What diagnoses are possible based on the *geographical areas* visited?
- What diagnoses are possible based on the time of travel (*incubation periods*)?
- What diagnoses are more likely based on activities, *exposures*, *host factors*, and *clinical and laboratory findings*?
- Among the possible diagnoses, what is/are *treatable*, *transmissible*, or both?

Gautret P, Parola P, Wilson ME. Fever in returned travelers. In: Keystone JS, Kozarsky P, Connor B, Nothdurft H, Leder K, Mendelson M (ed). *Travel Medicine*, 4th edition. Elsevier. 2019.

First principle:
Must recognize infectious disease emergencies



Strickland GT. *Hunter's Tropical Medicine and Emerging Infectious Diseases*. Saunders. 2000.

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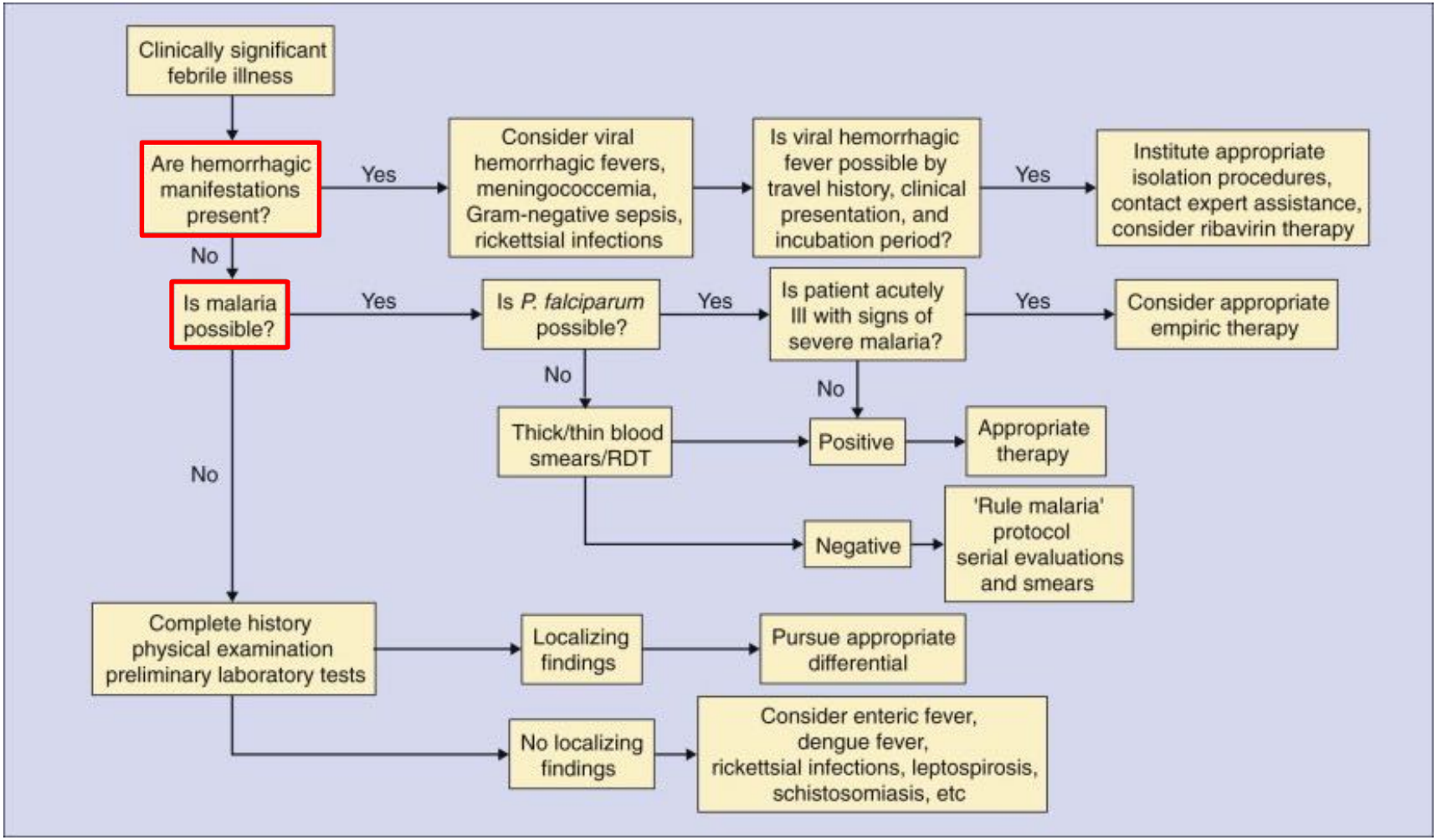


Wilson ME, Schwartz E, Parola P. Fever in returned travelers. In: Keystone JS, Freedman DO, Kozarsky PE, Connor BA, Nothdurft HD (ed). *Travel Medicine*, third edition. 2013, p. 475–485.

Recognize severe infections

- Clinical signs.
  - e.g. bleeding tendencies (petechiae, purpura), cyanosis, meningism, peritonism, oliguria/anuria, acral necrosis.
- qSOFA score (quick sequential organ failure assessment).
  - Glasgow coma scale <15.
  - Respiratory rate >22/min.
  - Systolic blood pressure <100 mmHg.

Paquet D, Jung L, Trawinski H, Wendt S, Lübbert C. Fever in the returning traveler. *Dtsch Arztebl Int* 2022;119:400–407.

Not necessarily travel-related or infectious

- Ubiquitous infections.
  - Viral respiratory tract infections, e.g. influenza, COVID, RSV.
  - Urinary tract infections, community-acquired pneumonia, meningitis, musculoskeletal and skin and soft tissue infections.
- Non-infective complications.
  - e.g. DVT, pulmonary embolism, drug reactions.

Emerging and re-emerging infections

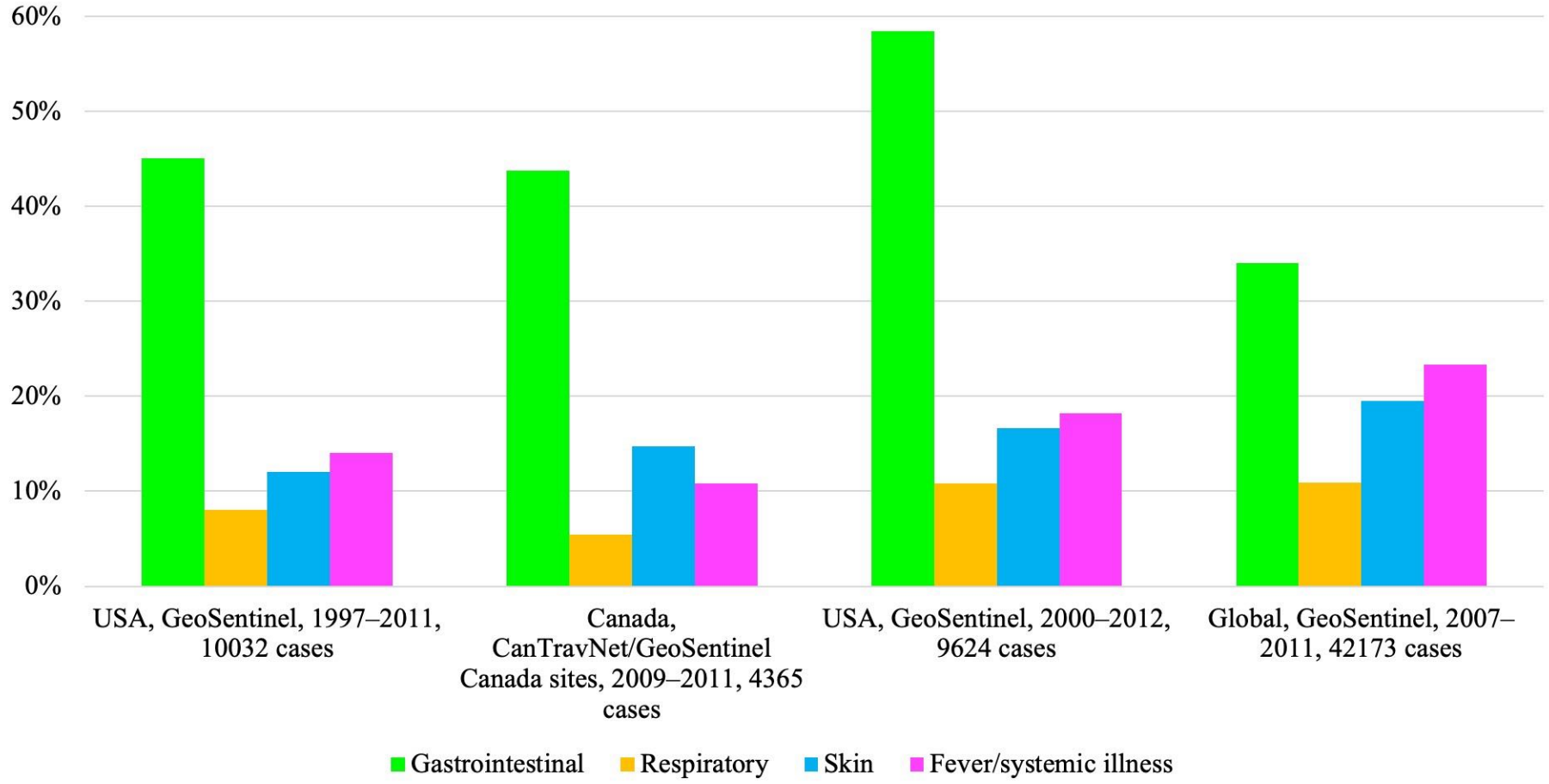
- Epidemic- or pandemic-prone infections.
  - e.g. SARS (2003), pandemic influenza (2009), MERS (since 2012), avian or animal influenza viruses, viral haemorrhagic fevers (e.g. Ebola, 2014), Zika virus infection (since 2015), COVID-19 (since 2020), monkeypox/Mpox (since 2022).
- Antibiotic-resistant bacteria.
  - e.g. ESBL- and carbapenemase-producing *Enterobacterales*, MRSA, VRE, multidrug-resistant *Acinetobacter baumannii* and *Pseudomonas aeruginosa*.
  - Highest risks in Indian subcontinent, Southeast Asia, Africa.
- *Candida auris.*
- Re-emerging infectious diseases.
  - e.g. measles in children and adults.
- Ectoparasitic infestations.
  - e.g. bedbugs.
- Infections with potential for local transmission.
  - e.g. malaria, dengue, chikungunya, viral haemorrhagic fevers, Zika virus infection.

Autochthonous infection of 'tropical' diseases in non-endemic areas

	Malaria	Dengue	Chikungunya	Urinary schistosomiasis
Europe	• Greece, France, Spain, Italy (2014–2021). • Belgium, 2 fatal cases of autochthonous airport malaria (2020).	• Croatia (2010). • Madeira, Portugal (2012). • France (2010, 2013, 2014, 2015, 2018, 2019, 2020, 2021, 2022, 2023 [Paris]). • Italy (2020, 2023). • Spain (2018, 2019, 2022, 2023).	• Italy (2007, 2017). • France (2010, 2014, 2017).	• Almería, Spain (2003). • Corsica, France (2011–2019).
USA	Texas, Florida, Maryland, Arkansas (2023).	• Hawaii (2001). • Texas (2005). • Florida (2009–2011). • Arizona (2022). • California (2023).	• Florida (2014). • Texas (2015).	
Japan		Tokyo (2014).		

Common infections and syndromes in the travellers

Illnesses in returned international travellers



Harvey K, Esposito DH, Han P, Kozarsky P, Freedman DO, Plier DA, Sotir MJ; Centers for Disease Control and Prevention (CDC). Surveillance for travel-related disease—GeoSentinel Surveillance System, United States, 1997–2011. *MMWR Surveill Summ* 2013;62:1–23.

Boggild AK, Geduld J, Libman M, Ward BJ, McCarthy AE, Doyle PW, Ghesquiere W, Vincelette J, Kuhn S, Freedman DO,Kain KC. Travel-acquired infections and illnesses in Canadians: surveillance report from CanTravNet surveillance data, 2009–2011. *Open Med* 2014;8:e20–32.

Hagmann SH, Han PV, Stauffer WM, Miller AO, Connor BA, Hale DC, Coyle CM, Cahill JD, Marano C, Esposito DH, Kozarsky PE; GeoSentinel Surveillance Network. Travel-associated disease among US residents visiting US GeoSentinel clinics after return from international travel. *Fam Pract* 2014;31:678–687.

Leder K, Torresi J, Libman MD, Cramer JP, Castelli F, Schlagenhauf P, Wilder-Smith A, Wilson ME, Keystone JS, Schwartz E, Barnett ED, von Sonnenburg F, Brownstein JS, Cheng AC, Sotir MJ, Esposito DH, Freedman DO; GeoSentinel Surveillance Network. GeoSentinel surveillance of illness in returned travelers, 2007–2011. *Ann Intern Med* 2013;158:456–468.

Travel-related infections

- Europe, EuroTravNet, 1998–2018.
  - 13 countries, 25 centres.
  - 103,739 ill travellers; 89.2% seen during or after travel.
  - Top diagnoses:
    - Acute diarrhea (9.3%).
    - Malaria (6.9%); falciparum malaria (4.4%).
    - Viral syndromes with or without rash (5.8%).
    - Dengue (3.6%).
    - Upper respiratory tract infections (2.1%).
  - Geographic variations in prevalence of diseases.
  - Deaths: 45 (0.04%).

Grobusch MP, Weld L, Goorhuis A, Hamer DH, Schunk M, Jordan S, Mockenhaupt FP, Chappuis F, Asgeirsson H, Caumes E, Jensenius M, van Genderen PJJ, Castelli F, López-Velez R, Field V, Bottieau E, Molina I, Rapp C, Ménendez MD, Gkrania-Klotsas E, Larsen CS, Malvy D, Lalloo D, Gobbi F, Florescu SA, Gautret P, Schlagenhauf P; for EuroTravNet. Travel-related infections presenting in Europe: A 20-year analysis of EuroTravNet surveillance data. *Lancet Reg Health Eur* 2020;1:100001.

Common considerations

- Enteric infections.
  - e.g. gastroenteritis, cholera, dysentery, giardiasis, amoebiasis, *Norovirus* and other enteric virus infections.
- Respiratory tract infections.
  - e.g. viral infections, pneumonia, legionellosis.
- Systemic infections.
  - Vectorborne diseases: e.g. malaria, rickettsioses, dengue, chikungunya, Zika virus infection.
  - Foodborne/waterborne diseases: e.g. enteric fever.
  - Zoonoses: e.g. brucellosis, Q fever.
  - Leptospirosis.
- Sexually-transmitted diseases, bloodborne viruses.
  - e.g. HIV, HBV, HCV, other sexually-transmitted infections.

Common infective syndromes

Common infective syndromes

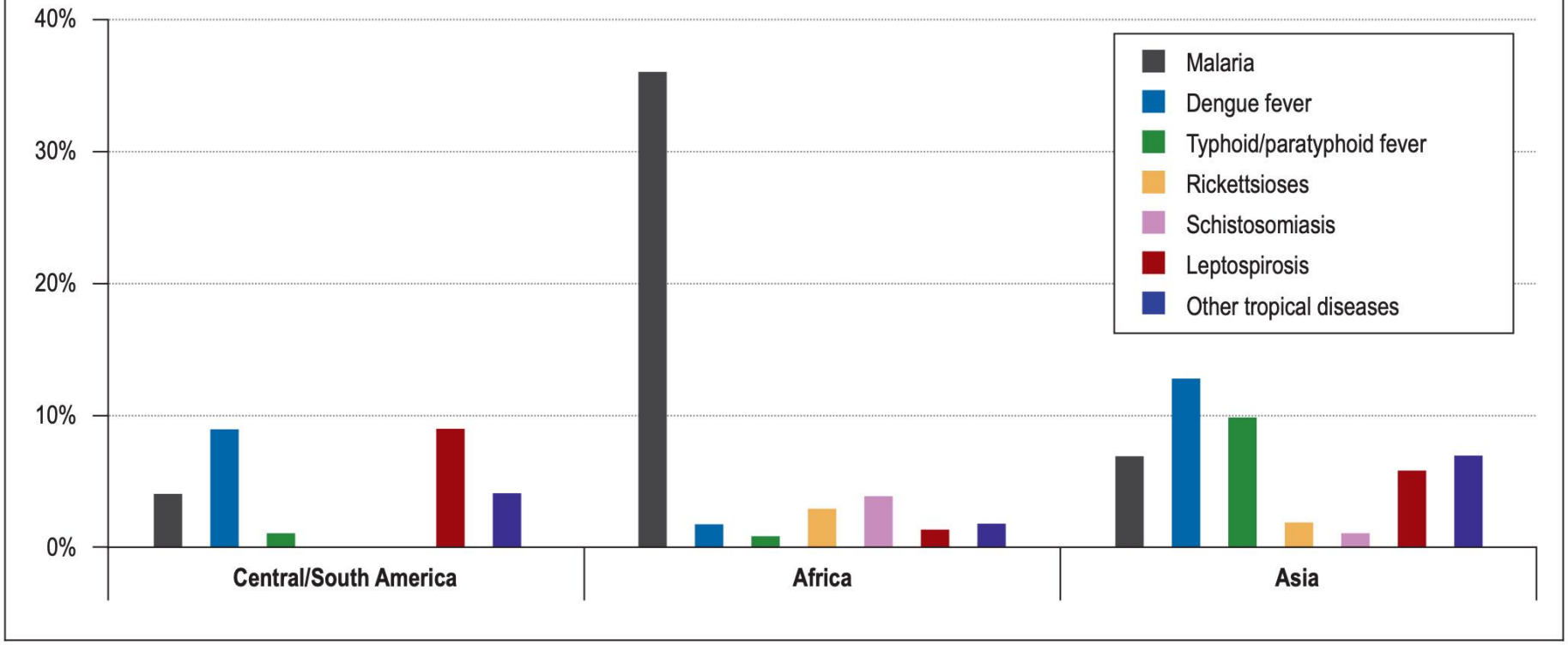
- Febrile syndromes.
  - Undifferentiated fever.
  - Fever + rash.
  - Fever + diarrhoea.
  - Fever + respiratory symptoms.
  - Fever + abdominal symptoms.
  - Fever + deranged liver functions.
  - Fever + neurological symptoms.
  - Fever + musculoskeletal symptoms.
  - Fever + haemorrhagic manifestation.
- Traveller's diarrhoea.
- Skin conditions.
- Eosinophilia.

Fever syndrome	Common pathogens
Fever without local symptoms	• Malaria (especially sub-Saharan Africa) • Dengue fever (especially Southeast Asia, South and Central America) • Typhoid and paratyphoid fever (especially Indian subcontinent) • Rickettsioses (especially sub-Saharan Africa)
Fever and rash (exanthema)	• Arboviral diseases (especially dengue, Chikungunya, Zika, and West Nile fever) • Viral HF, e.g. Ebola HF, Marburg HF • Measles, rubella, chickenpox, herpes zoster generalisatus (worldwide) • Acute HIV, EBV, CMV infection (mononucleosis syndrome) • Rickettsioses (eschar, rash); relapsing fever (especially tick-borne relapsing fever) • Typhoid fever (rose spots), syphilis (stage II) • African trypanosomiasis; acute schistosomiasis (urticaria) • Strongyloidiasis (urticaria, larva currens), trichinellosis (urticaria)
Fever and respiratory symptoms	• Influenza, COVID-19 (SARS-CoV-2) (worldwide) • MERS (MERS-CoV) (Arabian Peninsula) • Legionellosis (e.g., after cruise trip) • Melioidosis (especially Southeast Asia) • Tuberculosis (VFR, HCW), Q fever, psittacosis, leptospirosis • Acute histoplasmosis and coccidioidomycosis • Löffler syndrome and tropical pulmonary eosinophilia (helminth infection)
Fever and diarrhea	• Traveler's diarrhea, especially due to infection with ETEC, EAEC, EPEC, campylobacteriosis, salmonellosis, shigellosis, very rarely cholera • Norovirus, rotavirus enteritis (e.g., outbreaks on cruise ships) • Lambliasis/giardiasis, cryptosporidiosis (watery diarrhea) • Amoebic colitis (bloody diarrhea) • Malaria (in approx. 30% of cases watery diarrhea) • Typhoid fever (diarrhea starting week 2–3 of the disease)
Fever and abdominal pain	• Typhoid/paratyphoid fever • Lambliasis/giardiasis, cryptosporidiosis (upper abdominal pain, meteorism, nausea) • Pyogenic liver abscess or amebic liver abscess (hepatomegaly) • Brucellosis, malaria, visceral leishmaniosis (kala-azar), infectious mononucleosis (splenomegaly) • Relapsing fever (hepatosplenomegaly)
Fever and icterus	• Severe malaria (hemolysis), hepatitis A-E • Viral HF (yellow fever, Crimean–Congo HF, Rift Valley fever, severe dengue fever) • Leptospirosis (Weil's disease); bartonellosis (Oroya fever), HUS (e.g., EHEC) • Acute cholangitis (e.g., liver fluke infection)
Fever and hepatitis	• Hepatitis A-E, dengue fever • Acute CMV, EBV, HIV, toxoplasma gondii infection (mononucleosis syndrome) • Q fever, brucellosis, leptospirosis
Fever and neurological symptoms	• Bacterial meningitis (e.g., meningococcal, TB), typhoid/paratyphoid fever, neurosyphilis • Viral encephalitis (e.g., due to HSV, VZV, JE, WNV, dengue virus, rabies virus, measles, enteroviruses) • Cerebral malaria, African trypanosomiasis (sleeping sickness) • Angiostrongyliasis, gnathostomiasis (eosinophilic meningitis)
Fever and signs of bleeding (purpura)	• Sepsis (meningococcal, staphylococcal, streptococcal), rickettsioses, leptospirosis, plague • HF (e.g., Crimean-Congo HF, Ebola HF, Marburg HF, dengue HF, yellow fever)
Fever and eosinophilia	• Helminth infection, especially acute schistosomiasis, ascariasis, ancylostomiasis (hook worms), strongyloidiasis (Strongyloides stercoralis), fascioliasis (Fasciola hepatica), visceral larva migrans (toxocariasis), filariasis, trichinellosis
Fever and arthralgia or myalgia	• Chikungunya fever, dengue fever, Zika fever, Ross River fever (Australia), muscular sarcocystosis (Southeast Asia), trichinellosis

Watch the geography and exposure history too.

Paquet D, Jung L, Trawinski H, Wendt S, Lübbert C. Fever in the returning traveler. *Dtsch Arztebl Int* 2022;119:400–407.

eFIGURE 2



Frequency of occurrence of tropical diseases in the febrile returning traveler by travel region, adapted from (13)

Paquet D, Jung L, Trawinski H, Wendt S, Lübbert C. Fever in the returning traveler. *Dtsch Arztebl Int* 2022;119:400–407.

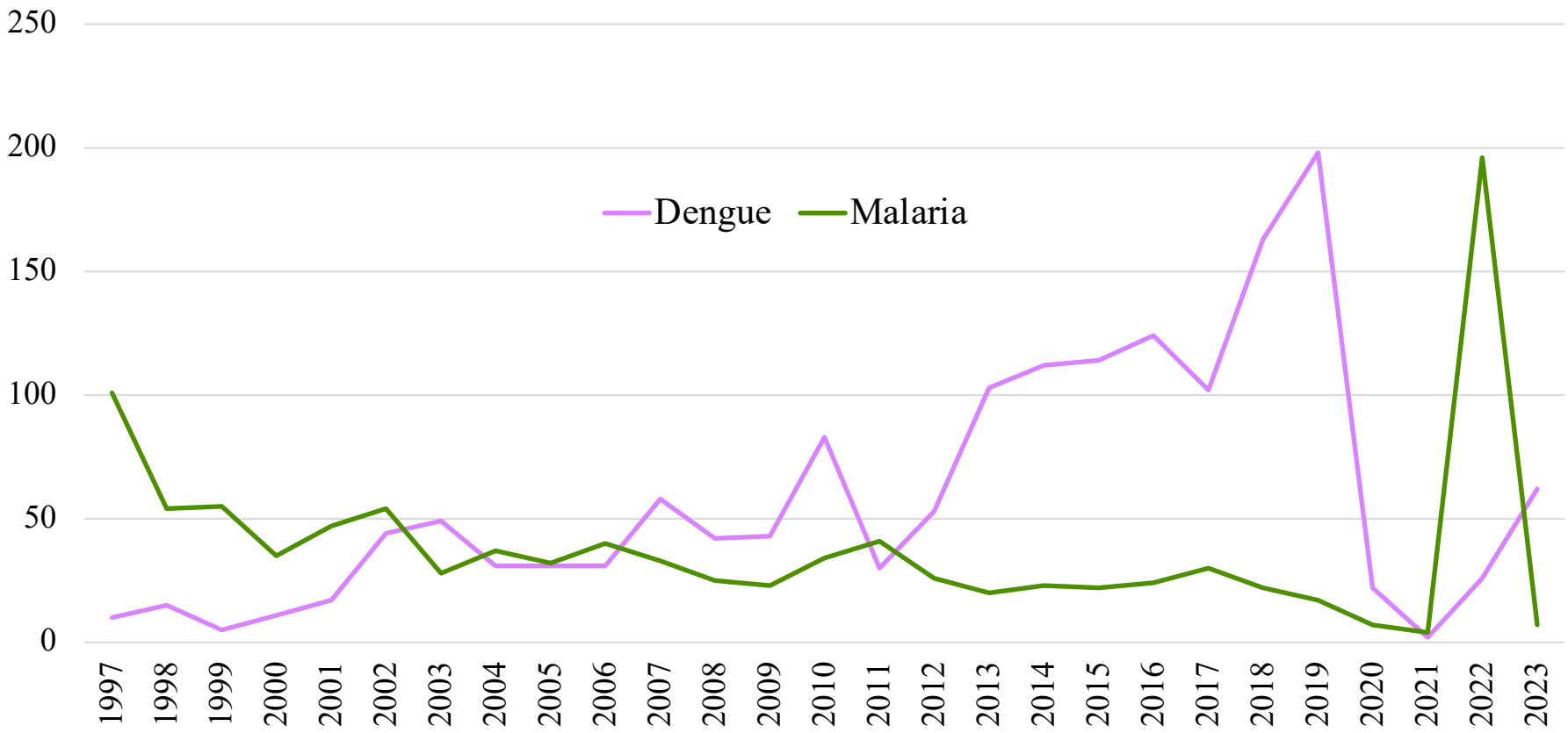
Fever in the returned traveller

- 2–10% of international travellers will experience a febrile illness either during their travel or within 2 weeks of returning from abroad.
  - 39% had fever abroad only.
  - 37% had fever abroad and at home.
  - 24% had fever at home only.
- Chief reason for seeking medical care in ~28% of returned travellers.

Causes of fever in returned international travellers

	Doherty, UK	MacLean, USA	O'Brien, Australia	Siikamäki, Finland	GeoSentinel	USA, GeoSentinel (1997–2011)	Canada, GeoSentinel (2009–2011)	USA, GeoSentinel (2000–2012)	Global, GeoSentinel (2007–2011)
Number of patients	195	587	232	462	6957	1802	675	1748	9817
Malaria	42%	32%	27%	4.3%	21%	19.4%	11.9%	27.4%	28.7%
RTI	2.6%	11%	24%	15%	14%		6.7%		
Diarrhoeal disease	6.7%	4.5%	14%	27%	15%				
Dengue	6.2%	2%	8%	2.8%	6%	11.1%	7.1%	12%	15.0%
Hepatitis	3%	6%	3%	0.4%	1%				1.7 (A, E)
Enteric fever	1.5%	2%	3%	1.1%	2%		4.1%	6.1%	4.8
UTI	2.6%	4%	2%	3.9%	2%		1.5%		
Rickettsioses	0.5%	1%	2%	1.3%	2%		0.7%	4.7%	3.0
Tuberculosis	1.6%	1%	0.4%	0.2%	0%		7%		
Amoebiasis	0%	1%	1%	0%	0.3%				
Systemic febrile illness				21%	22%	8.2%			
Skin infection				2.4%	4%				
No diagnosis	24.6%	25%	9%	25.1%	22%				
Chikungunya							0.9%		1.7
Viral syndrome						17.1%		18.5%	

Dengue and malaria in Hong Kong

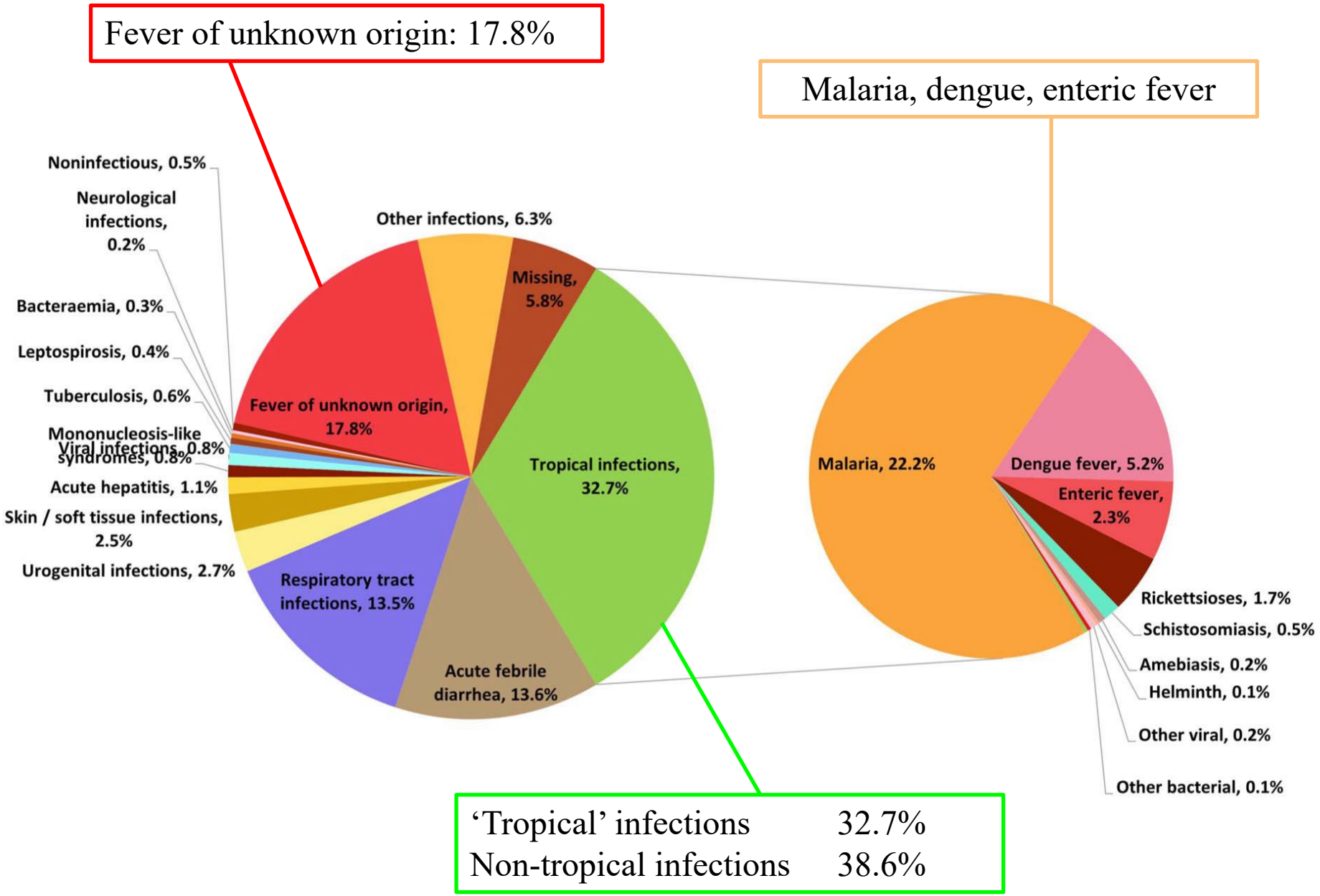


Department of Health.

Causes of fever in returned travellers

- 2001–2018.
- 30 studies on travellers and migrants (6%).
- 18,755 febrile patients.
- 32.3% febrile patients hospitalized (range 8.5–69.3%).
- Fatalities: 0.22%.
- Type of infections.
  - 'Tropical' infections 32.7%
  - Non-tropical infections 38.6%

Buss I, Genton B, D'Acremont V. Aetiology of fever in returning travellers and migrants: a systematic review and meta-analysis. *J Travel Med* 2020;27:taaa207.



Buss I, Genton B, D'Acremont V. Aetiology of fever in returning travellers and migrants: a systematic review and meta-analysis. *J Travel Med* 2020;27:taaa207.

When to suspect malaria?

- Clinical suspicion.
  - '*Malaria must be suspected in the differential diagnosis of any acute febrile illness in a patient who could have been exposed to malaria*.' (DA Warrell)
  - After 7 days of stay in an endemic area.
- Fever pattern.
  - Usually *not* helpful.
- EuroTravNet, 1998–2018.
  - Malaria patients: 2.5:1 risk ratio of dying compared to patients with all other diagnoses.

Warrell DA. Clinical features of malaria. In: Warrell DA, Gilles HM (ed). *Essential Malariology*, 4th edition. CRC Press. 2002.
Grobusch MP, Weld L, Goorhuis A, Hamer DH, Schunk M, Jordan S, Mockenhaupt FP, Chappuis F, Asgeirsson H, Caumes E, Jensenius M, van Genderen PJJ, Castelli F, López-Velez R, Field V, Bottieau E, Molina I, Rapp C, Ménendez MD, Gkrania-Klotsas E, Larsen CS, Malvy D, Lalloo D, Gobbi F, Florescu SA, Gautret P, Schlagenhauf P; for EuroTravNet. Travel-related infections presenting in Europe: A 20-year analysis of EuroTravNet surveillance data. *Lancet Reg Health Eur* 2020;1:100001.

Pitfalls in diagnosis

- Failure to elicit a history of exposure to malaria.
- Malaria never came into the differential diagnosis.
- Presence of localizing signs and symptoms diverted the diagnosis.
- Delays in starting antimalarial treatment; time wasted in waiting for transferal.
- Absence of fever or typical fever pattern excluded the possibility of malaria.
- Malaria considered unlikely because chemoprophylaxis was given.
- Initial negative investigation excludes the possibility of malaria.
- Delays in communication of laboratory findings with/between clinicians.
- Not recognizing the important clinical signs and laboratory findings.
- Long interval since last exposure and onset of symptoms.
- Other modes of transmission neglected.
- Malaria in temperate/malaria-free countries.

Table 3 Frequency of presenting symptoms

Symptom	Number of patients	(%)
Fever	49	(96)
Rigors/shivering	23	(45)
Headache	23	(45)
Vomiting	18	(35)
Arthralgia/myalgia	12	(24)
Sweats	9	(18)
Diarrhoea	8	(16)
Cough	7	(14)
Malaise	5	(10)
Abdominal pain	5	(10)
Periodic fever*	4	(8)
Sore throat	1	(2)
Loss of consciousness	1	(2)
No symptoms†	2	(4)

* Periodic (tertian) fever was only found in patients with benign malarias (3 vivax, 1 ovale). † 2 asymptomatic children had positive blood films when investigated after a sibling was admitted with symptomatic malaria.

51 malaria patients in Royal Free Hospital, 1991.

Brook MG, Bannister BA. The clinical features of imported malaria. *CDR Review* 1993;3:R28–R31.

Imported malaria (16 series)

- Predominant species.
  - *P. falciparum* in most overseas studies (origin: Africa).
- Most patients did not received/complete proper antimalarial prophylaxis.
- Clinical features.
  - Delayed diagnosis.
    - France, 1996–2003: 27,085 cases of malaria; median time from symptom onset to diagnosis = 3 days.
  - No pathognomonic signs and symptoms.
  - Periodic fever: 8–23% (2 series).
  - Can be confused with other infections.
    - Bacterial sepsis: coinfection possible.
    - Gastrointestinal or abdominal symptoms: 1–35%.
    - Respiratory symptoms: 6–20%.
  - Can be asymptomatic (1.5–4%).
  - Severe malaria: 0.8% to 36%.
  - Case-fatality ratio: 0% to ~10%.

Bacterial coinfections in malaria

Location	Population	Setting	Coinfection	Prevalence
Africa, 1992–2010, 25 studies	Children	Severe malaria	Invasive bacterial infections	6.4% (range 4.6–16.0%)
		All severity malaria	Invasive bacterial infections	3.0–24.7%
Vietnam, 1991–2003	Adults	Severe malaria	Bacteraemia	1.1%
Burma, 2014–2015	Adults	Falciparum malaria	Bacteraemia	13.4%
Burma, 2016–2017	Adults	Falciparum malaria	Bacteraemia	20.0%
Africa (44), Asia (6), Europe (1), 51 studies, 1993–2021	All	Falciparum malaria	Bacteraemia	7.6%
France, 1988–1999	Adults	Imported falciparum malaria in ICU, severe + non-severe	Bacteraemia Other bacterial infections	3.2% 9.0%
Sweden, 1995–2009	Adults	Imported malaria (*Pf* 59%; *Pv* 23%, *Po* 8%, others and mixed 10%).	Bacteraemia (55% had blood cultures taken)	0.5% of those with blood cultures taken
Germany, 2010–2019	Adults	Imported falciparum malaria, severe + non-severe	Bacterial infections Bacteraemia (83% had blood cultures taken)	11.0% 1.4% of those with blood cultures taken
France, Germany, Spain, Switzerland, UK, Singapore, South Africa, 13 studies, 1970–2011	Adults	Imported falciparum malaria in ICU	Bacterial infections Bacteraemia Community-acquired pneumonia	8% 3% 3%

Undifferentiated fever

- Malaria.
- Enteric fever.
- Arbovirus infections.
  - e.g. dengue, chikungunya, Zika.
- Rickettsioses.
- Leptospirosis.
- Bacterial sepsis.
- Amoebic liver abscess.

… …

Fever + rash

- Arbovirus infections.
- Rickettsioses.
- Leptospirosis.
- Enteric fevers (paratyphoid, typhoid).
- ‘Childhood’ exanthemata, e.g. measles, rubella, varicella.
- Less common:
  - Secondary syphilis.
  - Primary HIV infection.
  - Meningococcaemia, gonococcaemia.
  - Viral haemorrhagic fevers.
  - Acute schistosomiasis.
  - Strongyloidiasis.
  - Human African trypanosomiasis.
- Drug reactions.

Travel-associated legionellosis

- EU/EEA.
  - 2019: 14.7%.
  - 2021: 8.3%.
  - Destinations with highest number of cases: Italy, France, Spain.
- England and Wales.
  - 2019: 50.0%.
- USA.
  - 1980–1998: 20.8%
  - 2005–2009: 24.0%
  - 2015–2016: 12.3%.
- Hong Kong.
  - 2018: 10.5%

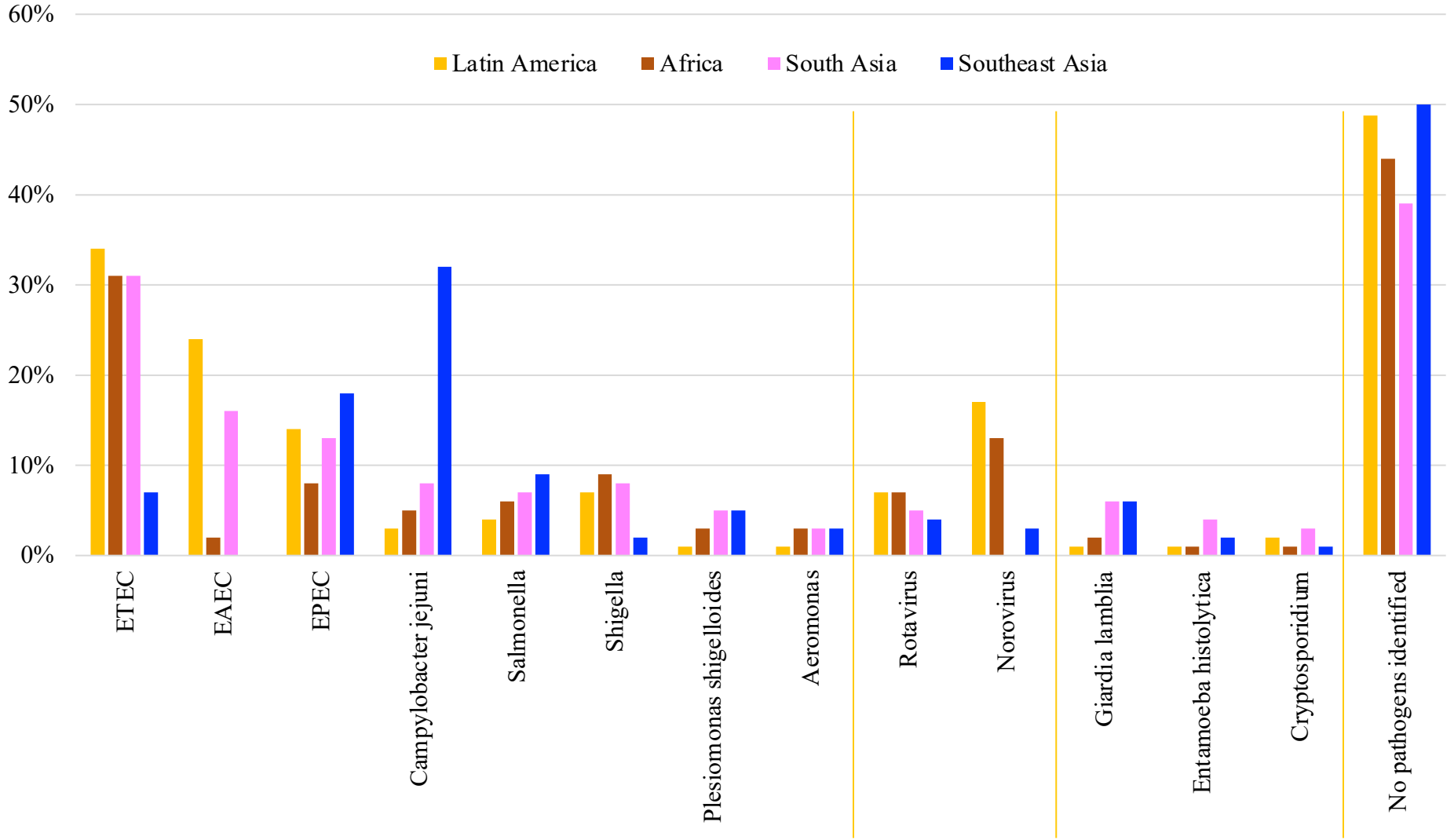
European Centre for Disease Prevention and Control. *Legionnaires' disease. Annual Epidemiological Report for 2019.*
European Centre for Disease Prevention and Control. *Legionnaires' disease. Annual Epidemiological Report for 2021.*
https://assets.publishing.service.gov.uk/media/5e259873ed915d1f26a741e2/Monthly_LD_Report_December_2019.pdf
Benin AL, Benson RF, Besser RE. Trends in legionnaires disease, 1980-1998: declining mortality and new patterns of diagnosis. *Clin Infect Dis* 2002;35:1039–1046.
Centers for Disease Control and Prevention (CDC). Legionellosis — United States, 2000–2009. *MMWR Morb Mortal Wkly Rep* 2011;60:1083–1086.
Barskey AE, Lackraj D, Tripathi PS, Lee S, Smith J, Edens C. Travel-associated cases of Legionnaires' disease in the United States, 2015–2016. *Travel Med Infect Dis* 2021;40:101943.
Centre for Health Protection. *Communicable Disease Watch* 2019 Feb 10 – Feb 23.

Traveller's diarrhoea

- Occurrence.
  - ~50% (30–80%) travellers from industrialized to developing countries during the first 2 weeks of travel.
  - 90% in the first 2 weeks, especially first 3–4 days.
- Impact.
  - 12–46% changed itinerary.
  - 10–20% confined to bed.
  - 0.1–0.4% hospitalized.
- Mean duration: 3–4 days.
  - 10% last >1 week.
  - 2% last >1 month.
  - <1% last >3 months.
- To perform laboratory investigations or not?
  - Duration of symptoms.
  - Severity of the illness.
  - Type of diarrhoea (inflammatory vs. non-inflammatory).
  - Host factors.

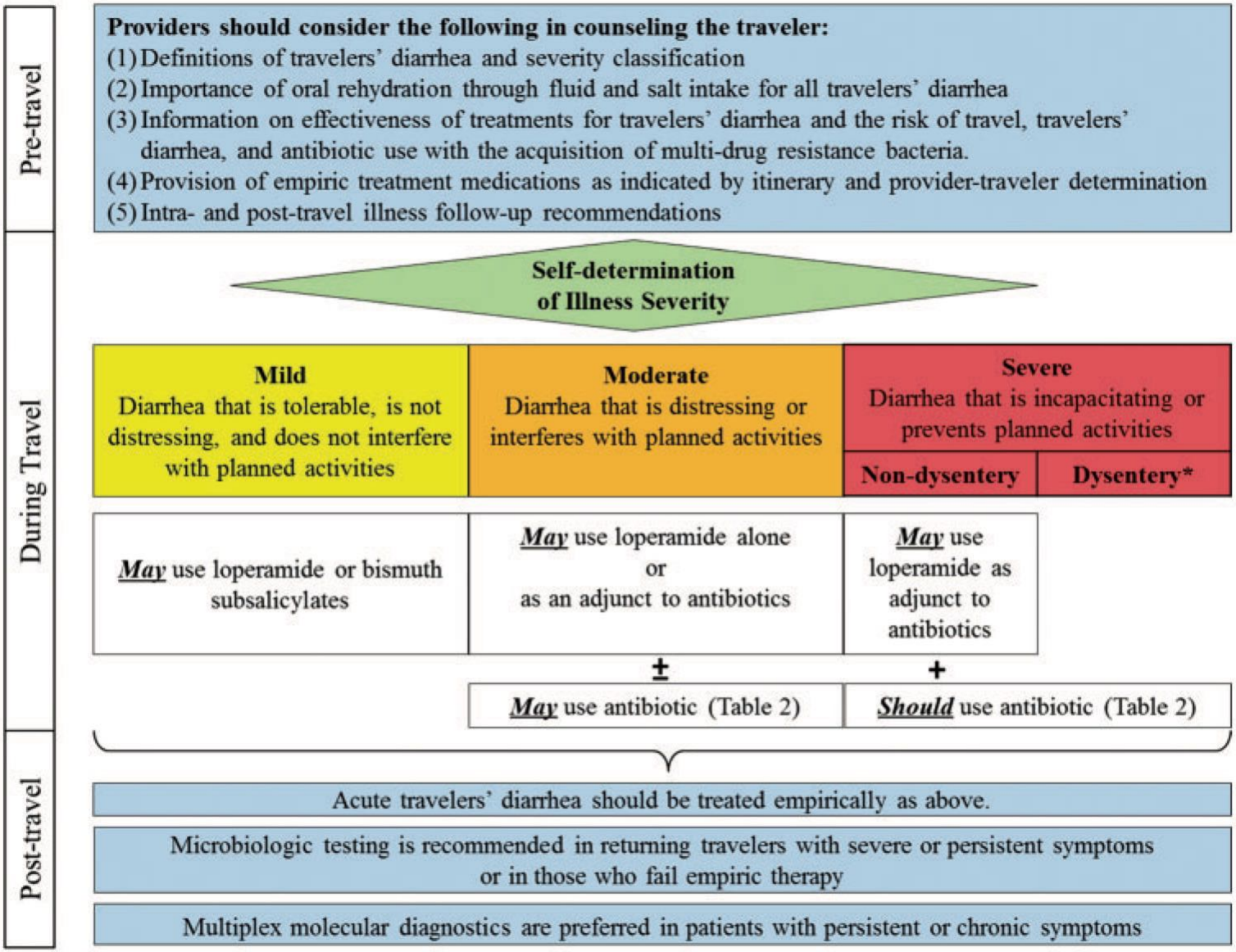
Steffen R. Epidemiology of travellers' diarrhea. *J Travel Med* 2017;24(suppl_1):S2–S5.

Pathogens in travellers' diarrhoea



Ericsson CD. Travellers' diarrhoea. In: Zuckerman JN (ed). *Principles and Practice of Travel Medicine*, second edition. Blackwell Publishing Ltd. 2013. pp 197–208.

Management of travellers' diarrhoea



Azithromycin
Ciprofloxacin
Levofloxacin
Ofloxacin
Rifaximin

Riddle MS, Connor BA, Beeching NJ, DuPont HL, Hamer DH, Kozarsky P, Libman M, Steffen R, Taylor D, Tribble DR, Vila J, Zanger P, Ericsson CD. Guidelines for the prevention and treatment of travelers' diarrhea: a graded expert panel report. *J Travel Med* 2017;24(suppl_1):S57–S74.

Skin problems

- Infections.
  - Pyoderma, skin abscesses, cellulitis.
  - Cutaneous larva migrans.
  - Myiasis.
  - Tungiasis.
  - Cutaneous diphtheria, Buruli ulcer.
- Envenoming, arthropod bites and stings, jellyfish.
- Body modification and medical tourism.
  - Non-tuberculous mycobacteria (e.g. *Mycobacterium abscessus*), fungi, *Nocardia*.
- Cutaneous manifestations of systemic infections.
- Non-infections.
  - Sunburn.
  - Drug eruptions.
  - Other dermatitis.

Skin manifestations of systemic infections

Manifestation	Differential diagnoses
Haemorrhagic pustules	Meningococcaemia, gonococcaemia.
Panniculitis	Tuberculosis, others.
Ecthyma gangrenosum	*Pseudomonas aeruginosa* and others.
Erythema multiforme	*Mycoplasma pneumoniae*, *Herpesviridae*, other viral infections.
Eschar	Rickettsioses.
Fever + rash	Rickettsioses, leptospirosis, syphilis, Lyme disease, dengue, infective endocarditis, scarlet fever, enteric fever, rheumatic fever, toxic shock syndrome, staphylococcal scalded skin syndrome.
Viral exanthemata	Measles, rubella, chickenpox, erythema infectiosum (fifth disease, parvovirus B19), hand, foot, and mouth disease, roseola infantum (HHV-6).

Watch out for potentially life-threatening infections.

Travel-related infections

- Take a proper travel and exposure history.
- Don’t dismiss potentially important travel history.
- Watch out for ‘high consequence infectious diseases’ (highly contagious, life-threatening).
- Recognize important clinical syndromes and common aetiologies.

Some useful information

- WHO, infectious disease outbreak news.
  - https://www.who.int/emergencies/disease-outbreak-news
- CDC, travellers' health.
  - https://wwwnc.cdc.gov/travel/
- GeoSentinel alerts.
  - https://geosentinel.org/alerts
- ProMED.
  - https://promedmail.org/
- TRAVAX.
  - https://www.travax.nhs.uk/outbreaks-index/