

Travel Medicine

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Overview

- Travel Medicine background
- Travel Medicine at Hennepin Healthcare
- Pre travel consultation
- Post travel infection concerns

No conflicts of interest to report

International travel background

- International travel is increasing
  - 435 million in 1990 → 1.2 billion travelers in 2015
  - Trips to developing regions increased 31% → 47% of all travel
- Reason for travel is changing
  - Tourism ↓, visiting friends and relatives ↑
    - ~ 150 million people live outside their birth country
  - 14% of US college students study abroad, 46% in non-European country
  - Medical tourism
- Only 44% of international travelers from the US see a medical provider prior to travel
  - Only 10-20 % of these in a dedicated travel clinic
    - More errors occur with travel advice from non travel clinics
    - Travel services may be limited

Leder Emerg Infect Dis 2013;19:1049-57.
Harvey MMWR 2013;63:1-23.
Thwaites N Engl J Med 2017;376:548-60.

International travel map

The next infectious disease outbreak is just a plane ride away…

Recent travel related concerns

- Travelers contribute to the global spread of infectious diseases, including novel/emerging diseases
  - **Zika**
  - Chikungunya
  - **MERS-CoV**
  - SARS
  - **Measles**
  - **Viral hemorrhagic fevers (Ebola)**
  - **Multidrug resistant organisms (MDROs)**

COVID-19

- Drastic and precipitous decrease in travel
  - During 2020, US TSA screened 39% of the number passengers that were screened during 2019
  - November 2020: London Heathrow Airport, Frankfurt Airport, and Singapore Changi Airport were approximately 12%, 13%, and 1.9% (respectively) of the number of passengers compared to November 2019.
- Travel returning, but new and changing challenges
  - COVID testing for entry
  - Vaccination?

HCMC International Travel Medicine Clinic

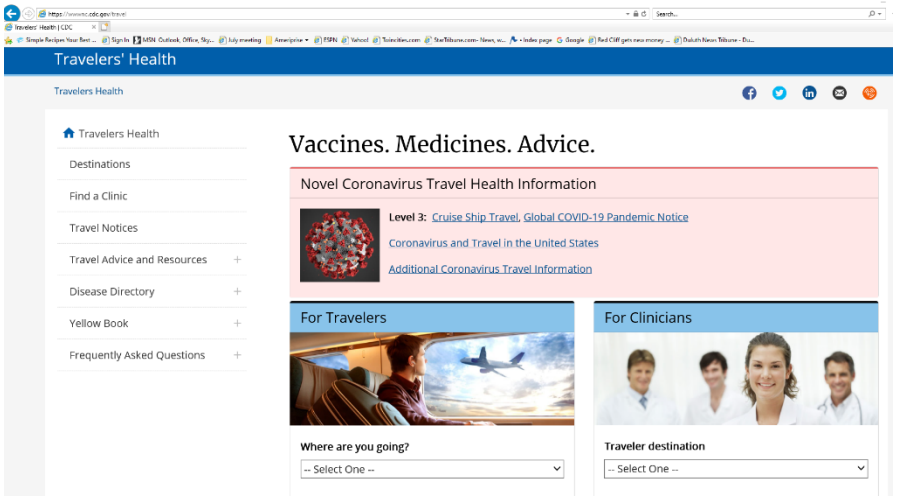
- Sees patients of all ages, including families traveling together
  - In person and now telephone visits
- Providers who are ID trained who are available for post travel related infection concerns
- Dedicated clinic staff (RN, MA, providers)
- Specialty pharmacy partner
- Provides travel related vaccines and medications, including YF vaccine (formerly a Stamaril EAP site)
- Now provides COVID-19 PCR testing with < 24 hour turnaround time
- Clinic back line for providers/clinic staff: *redacted for posting*

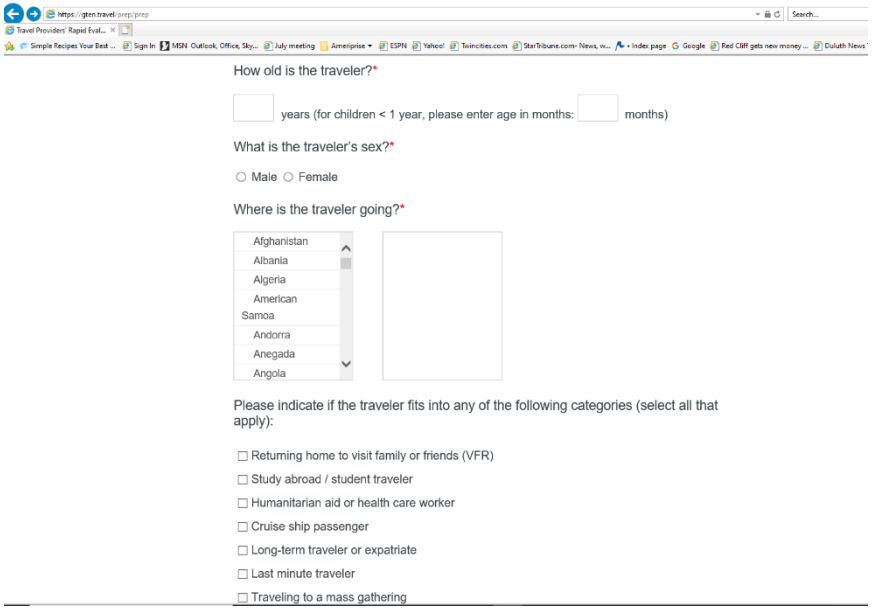
Travelers in primary care clinics

- When possible- refer to travel clinic!
  - Make sure routine immunizations are up to date
  - Delay live virus vaccines in case others (YF) needed at travel visit, unless long duration prior to travel
  - Check titers if unknown status for hepatitis A, B, MMR, varicella
- What to do if travel clinic referral not possible?!?
  - Call!
  - Consult your resources

Travel resources

- www.cdc.gov/travel
- Global TravEpiNet (http://gten.travel/prep/prep)
- www.headinghomehealthy.org
- Shoreland Travax
- CDC Yellow book
- Travel Medicine, Jay Keystone
- Oxford Handbook of Tropical Medicine





Pre travel consultation

- Components of a pre travel visit:
  - Assessing risk
  - Counseling on medical conditions
  - Counseling on travel related issues
  - Medications
  - Vaccines

Assessing risk

- Patient specific
  - Age, medical history, medications, allergies, pregnancy, etc.
- Trip specific
  - Departure date, length of stay
  - Destination(s), urban vs rural
  - Reason for travel
  - Lodging
  - Food
  - Transportation
  - Activities

Special travel populations

- Visiting friends and relatives (VFR)
  - Refers to immigrants ethnically/racially distinct from the majority population of their country of residence who return home to visit friends and/or relatives
  - Typically traveling from high-income to low-income country
  - Most commonly travel to Sub-Saharan Africa
  - Duration between immigration and travel back to home country varies widely, but most often > 4 years
    - Waning malaria immunity
  - Includes second generation immigrants who were born in the country of residence
    - Younger age
    - Risks are slightly different than first generation

VFR travelers

- Increased exposure to pathogens
  - Staying in remote rural areas
  - Close contact with local population
  - High-risk food/beverages
- Less likely to seek pre-travel advice (only 16%)
  - Less likely to receive travel vaccinations
  - Less likely to take malaria chemoprophylaxis
- Last minute travel
- More prolonged stay in visiting country

Special travel populations

Immunocompromised travelers: HIV/AIDs, transplant, steroids/anti-TNF, etc.

- 2015 study: 60% had traveled internationally in past 10 years, 45% to high risk destinations

- Areas of concern
  - Travel may cause problems with underlying disease
  - Host country may not be able to provide needed medical care
  - May be unable to receive live vaccinations, decreased response to other vaccines
  - Travel related medications may interact with chronic medications
  - May be more susceptible to infection and/or more severe manifestations of infection
- Need early referral to travel clinic

Bialy Intern Med J 2015

Special travel populations

- Pediatric travelers
  - Incomplete routine vaccine series
  - Too young for recommended vaccines
  - Dosing/administrations of medications
  - Increased risk of travelers' diarrhea, including severe dehydration
  - More severe manifestations of other diseases

Special travel populations

Pregnant travelers

- 2nd trimester generally regarded as safest for travel
- Potential contraindications for travel
  - Medical risk factors
  - OB risk factors
  - Destination specific factors
- Complicating factors
  - Live virus vaccines
  - Malaria prophylaxis
  - Travelers diarrhea
  - Unique, higher risk pathogens
- Similar complications/considerations for breast feeding travelers

Counseling on chronic conditions

- Notification of PCP and/or specialists
- Full supply of chronic medications
- Medication letter, especially if controlled substances
- Epi pen
- Anticipation/planning for potential problems
- Medical care at destination
- Overseas medical and evacuation insurance

Counseling on travel related issues

- **Food/Water safety**
- **Insect avoidance**
- **Animal bites**
- **Road safety, other safety concerns**
- DVT prevention
- Water
- Altitude
- Sea sickness
- Motion sickness
- Jet lag
- STDs/high risk behaviors
- Medical care while abroad
- Cruise ships
- Mass gatherings

Medications

- Medical kit of OTC medications
  - Pain/fever meds, antidiarrheal, constipation, antacids, antihistamine, decongestants, creams (hydrocortisone, antifungal), etc.
- Preventative medications
  - Malaria chemoprophylaxis: atovaquone-proguanil (malarone), mefloquine, doxycycline, [tafenoquine]
  - Altitude: acetazolamide (Diamox)
  - Sea sickness/Motion sickness: scopolamine, meclizine
  - HIV: PEP (truvada + dolutegravir) OR PrEP (truvada)
- Self treatment
  - Travelers diarrhea
  - Yeast infections
  - Symptom based treatment for malaria (if chemoprophylaxis not an option)

Malaria chemoprophylaxis

Table 4–10. Drugs used in the prophylaxis of malaria

DRUG	USAGE	ADULT DOSE	PEDIATRIC DOSE	COMMENTS
Atovaquone-proguanil	Prophylaxis in all areas	Adult tablets contain 250 mg atovaquone and 100 mg proguanil hydrochloride. 1 adult tablet orally, daily	Pediatric tablets contain 62.5 mg atovaquone and 25 mg proguanil hydrochloride. 5–8 kg: 1/2 pediatric tablet daily >8–10 kg: 3/4 pediatric tablet daily >10–20 kg: 1 pediatric tablet daily >20–30 kg: 2 pediatric tablets daily >30–40 kg: 3 pediatric tablets daily >40 kg: 1 adult tablet daily	Begin 1–2 days before travel to malarious areas. Take daily at the same time each day while in the malarious area and for 7 days after leaving such areas. Contraindicated in people with severe renal impairment (creatinine clearance <30 mL/min). Atovaquone-proguanil should be taken with food or a milky drink. Not recommended for prophylaxis for children weighing <5 kg, pregnant women, and women breastfeeding infants weighing <5
Doxycycline	Prophylaxis in all areas	100 mg orally, daily	≥8 years of age: 2.2 mg/kg up to adult dose of 100 mg/day	Begin 1–2 days before travel to malarious areas. Take daily at the same time each day while in the malarious area and for 4 weeks after leaving such areas. Contraindicated in children <8 years of age and pregnant women.
Mefloquine	Prophylaxis in areas with mefloquine-sensitive malaria	228 mg base (250 mg salt) orally, once/week	≤9 kg: 4.6 mg/kg base (5 mg/kg salt) orally, once/week >9–19 kg: 1/4 tablet once/week >19–30 kg: 1/2 tablet once/week >30–45 kg: 3/4 tablet once/week >45 kg: 1 tablet once/week	Begin ≥2 weeks before travel to malarious areas. Take weekly on the same day of the week while in the malarious area and for 4 weeks after leaving such areas. Contraindicated in people allergic to mefloquine or related compounds (quinine, quinidine) and in people with active depression, a recent history of depression, generalized anxiety disorder, psychosis, schizophrenia, other major psychiatric disorders, or seizures. Use with caution in people with psychiatric disturbances or a previous history of depression. Not recommended for people with cardiac conduction abnormalities.

Malaria chemoprophylaxis

Chloroquine	Prophylaxis only in areas with chloroquine-sensitive malaria	300 mg base (500 mg salt) orally, once/week	5 mg/kg base (8.3 mg/kg salt) orally, once/week, up to maximum adult dose of 300 mg base	Begin 1–2 weeks before travel to malarious areas. Take weekly on the same day of the week while in the malarious area and for 4 weeks after leaving such areas. May exacerbate psoriasis.
Primaquine[1]	Prophylaxis for short-duration travel to areas with principally *P.vivax*	30 mg base (52.6 mg salt) orally, daily	0.5 mg/kg base (0.8 mg/kg salt) up to adult dose orally, daily	Begin 1–2 days before travel to malarious areas. Take daily at the same time each day while in the malarious area and for 7 days after leaving such areas.
	Presumptive antirelapse therapy (PART or terminal prophylaxis) to decrease the risk for relapses of *P. vivax* and *P. ovale*	30 mg base (52.6 mg salt) orally, daily	0.5 mg/kg base (0.8 mg/kg salt) up to adult dose orally, daily	PART indicated for people with prolonged exposure to *P. vivax, P. ovale,* or both: daily for 14 days after departure from the malarious area. Contraindicated in people with G6PD deficiency. Also contraindicated during pregnancy and lactation, unless the infant being breastfed has a documented normal G6PD level.
Tafenoquine[1]	Prophylaxis in all areas	200 mg orally	Not indicated in children <16 years old	Begin taking daily for 3 days prior to travel to malarious areas. Then, take weekly while at the malarious area, and for 1 week after leaving the malarious area.
	Presumptive antirelapse therapy (PART or terminal prophylaxis) to decrease the risk for relapses of *P. vivax* and *P. ovale*	300mg orally	300mg orally	PART indicated for people who had prolonged exposure to *P. vivax, P. ovale* or both: Administered as a single dose. Contraindicated in people with G6PD deficiency. Also contraindicated during pregnancy and lactation unless the infant being breastfed has a documented normal G6PD level

Abbreviation: PART, presumptive antirelapse therapy.
[1] All people who take primaquine or tafenoquine should have a documented normal G6PD level before starting the medication.

Travelers' diarrhea

- Most common condition reported by travelers
- 30-70% of travelers, depending on the destination
  - Low risk countries: US, Canada, Australia, New Zealand, Japan, northern and western Europe
  - Intermediate risk countries: Eastern Europe, South Africa, Caribbean islands
  - High risk areas: Asia, Africa, the Middle East, Mexico, Central and South America
- Risk factors: from high-income countries, children/young adults , reduced gastric acid, adventure tourists, low cost accommodation, cruise ships
- Consuming fecally contaminated food/water
- Hand hygiene practices of traveler, people at destination (restaurants, etc.)

Etiology of travelers' diarrhea

- 80-90% Bacterial pathogens
  - *E. coli* (enterotoxogenic)
  - *Campylobacter jejuni*
  - *Shigella* spp.
  - *Salmonella* spp.
- 5-8% Viral pathogens
  - Norovirus, rotavirus, astrovirus
- Protozoan pathogens
  - *Giardia intestinalis*
  - *Cyclospora cayetanensis* in certain regions: Nepal, Peru, Haiti, Guatemala
  - *Entamoeba histolytica, Cryptosporidium parvum:* uncommon in travelers
  - Others: *Isospora, Microsporidia, Dientamoeba fragillis*

Symptoms

- Incubation period
  - 6-48 hours for bacterial, viral
  - 1-2 weeks for protozoa
- Duration (without treatment)
  - Bacterial: 3-5 days
  - Viral: 2-3 days
  - Protozoa: weeks to months
- Malaise, anorexia, abdominal cramps, watery diarrhea, nausea/vomiting (10-25%, especially viral)

Travelers' diarrhea and fever

- 1/3 of patients with travelers diarrhea have low grade fever
- Dysentery: fever, bloody stool
  - ***Shigella***
  - ***Campylobacter***
  - Enterohaemorrhagic *E. coli*
  - *Salmonella*
  - *Yersina*
  - *E. histolytica*
  - *Clostridium difficile*

Travelers diarrhea self treatment

Table 2–10. Travelers' diarrhea treatment recommendations

Therapy of mild travelers' diarrhea

- Antibiotic treatment is not recommended in patients with mild travelers' diarrhea.
- Loperamide or BSS may be considered in the treatment of mild travelers' diarrhea.

Therapy of moderate travelers' diarrhea

- Antibiotics may be used to treat cases of moderate travelers' diarrhea.
- Fluoroquinolones may be used to treat moderate travelers' diarrhea.
- Azithromycin may be used to treat moderate travelers' diarrhea.
- Rifaximin may be used to treat moderate, noninvasive travelers' diarrhea.
- Loperamide may be used as adjunctive therapy for moderate to severe travelers' diarrhea. Antimotility agents alone are not recommended for patients with bloody diarrhea or those who have diarrhea and fever.
- Loperamide may be considered for use as monotherapy in moderate travelers' diarrhea.

Therapy of severe travelers' diarrhea

- Antibiotics should be used to treat severe travelers' diarrhea.
- Azithromycin is preferred to treat severe travelers' diarrhea.
- Fluoroquinolones may be used to treat severe, nondysenteric travelers' diarrhea.
- Rifaximin may be used to treat severe, nondysenteric travelers' diarrhea.[1]
- Single-dose antibiotic regimens may be used to treat travelers' diarrhea.

[1] These treatment recommendations were developed prior to the approval of rifamycin SV in the United States. Because it is in the same category of antimicrobial drug as rifaximin and because they have the same mechanism of action, rifamycin SV can be considered as an alternative to rifaximin.

Increasing risk of MDRO colonization!

Vaccines

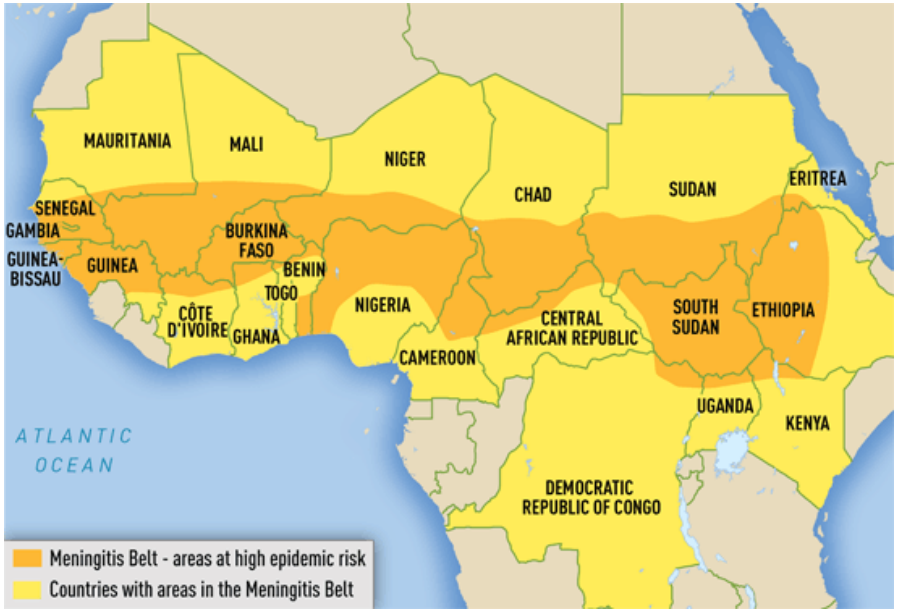
- Catch up to date on routine vaccines!
  - Influenza
  - Hepatitis A/B
  - MMR
  - Tdap
  - Polio
  - Pneumococcus
  - Varicella/Zoster
- May need titers: Hepatitis A/B, MMR, Varicella
- Pediatric travelers: early vaccination for Hepatitis A, MMR, Varicella

Travel vaccines

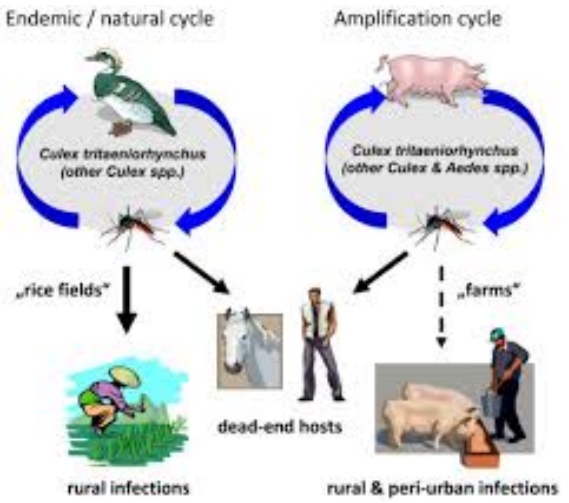
- Hepatitis A: 2 dose series (0, 6 months)
  - licensed age 12 months and up; Now recommended for age 6-11 months but doesn't count towards routine series
  - Routinely given in US childhood vaccination series since 2008
- Typhoid
  - IM: inactive vaccine, 2-3 years protection, ≥ 2 yrs
  - Oral: live, 5 years protection, more effort by patient, ≥ 6 yrs
- Polio booster
  - Some countries require 1 adult booster, document on ICVP ("yellow card")
- Rabies
  - Pre exposure series: 0, 7, 21-28 days. Eliminates need for RIG and fewer post exposure vaccines
- Cholera vaccine
  - Available for adults but limited use

Meningococcal vaccines

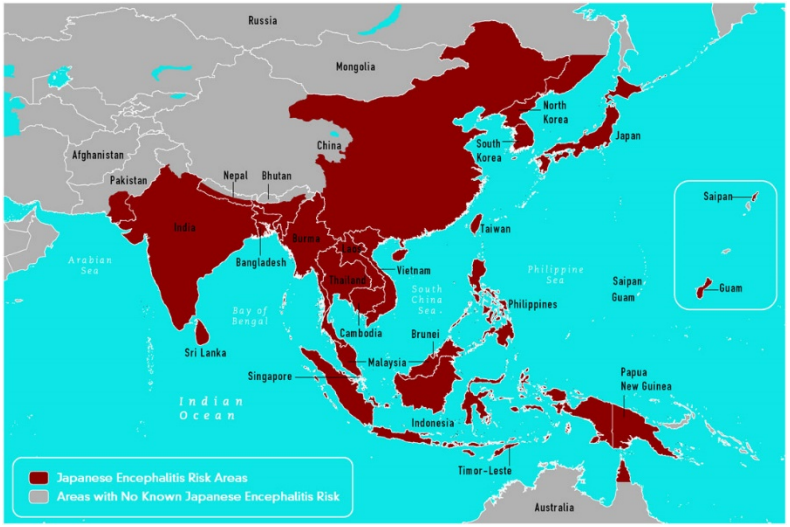
- Conjugate vaccines
  - Menactra (9 mo – 55 yrs)
  - Menveo (2 mo – 55 yrs)
- Common off label use in adults > 55 years of age
- Meningitis belt of Africa
- Required for Hajj travelers
  - Document on ICVP ("yellow card")
- Booster every 5 years (more frequently for younger children)



Japanese encephalitis (JE)

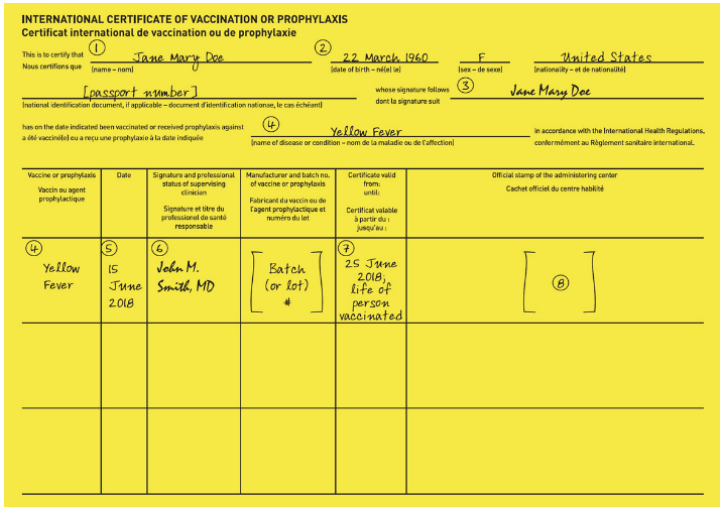


- Mosquito vector (daytime)
- True incidence of infection in endemic countries unknown
  - Potential for long term neurological sequela
- Rarely reported in travelers
- JE vaccine (Ixiaro)
  - 0, 28 days. Booster at 1 yr
    - Can accelerate to 0, 7 days for adults
  - Select travelers? Prolonged stays, rural areas
  - Expensive!



Yellow fever vaccine

- Live virus vaccine with rare, serious side effects
  - Viscerotropic or neurotropic disease (1-2 in 125,000 administered doses)
- Age 9 mo and above, precaution > 60 yrs
- Can only be given at licensed clinics, ICVP documentation
- Lifetime protection (previously 10 yr booster) unless immunocompromised



INTERNATIONAL CERTIFICATE OF VACCINATION OR PROPHYLAXIS
Certificat international de vaccination ou de prophylaxie

This is to certify that / Nous certifions que: ① Jane Mary Doe (name – nom); ② 22 March 1960 (date of birth – né(e) le); F (sex – de sexe); United States (nationality – et de nationalité)

[passport number] (national identification document, if applicable – document d'identification nationale, le cas échéant); whose signature follows / dont la signature suit: ③ Jane Mary Doe

has on the date indicated been vaccinated or received prophylaxis against / a été vacciné(e) ou a reçu une prophylaxie à la date indiquée: ④ Yellow Fever (name of disease or condition – nom de la maladie ou de l'affection)

in accordance with the International Health Regulations. / conformément au Règlement sanitaire international.

Vaccine or prophylaxis / Vaccin ou agent prophylactique	Date	Signature and professional status of supervising clinician / Signature et titre du professionnel de santé responsable	Manufacturer and batch no. of vaccine or prophylaxis / Fabricant du vaccin ou de l'agent prophylactique et numéro du lot	Certificate valid from: until: / Certificat valable à partir du : jusqu'au :	Official stamp of the administering center / Cachet officiel du centre habilité
④ Yellow Fever	⑤ 15 June 2018	⑥ John M. Smith, MD	[Batch (or lot) #]	⑦ 25 June 2018; life of person vaccinated	[⑧]

Table 4-23. Countries with risk of yellow fever (YF) virus transmission[1]

AFRICA			CENTRAL AND SOUTH AMERICA
Angola	Ethiopia[2]	Nigeria	Argentina[2]
Benin	Gabon	Senegal	Bolivia[2]
Burkina Faso	The Gambia	Sierra Leone	Brazil[2]
Cameroon	Ghana	South Sudan	Colombia[2]
Central African Republic	Guinea	Sudan[2]	Ecuador[2]
Chad[2]	Guinea-Bissau	Togo	French Guiana
Congo, Republic of the	Kenya[2]	Uganda	Guyana
Côte d'Ivoire	Liberia		Panama[2]
Democratic Republic of the Congo[2]	Mali[2]		Paraguay
Equatorial Guinea	Mauritania[2]		Peru[2]
	Niger[2]		Suriname
			Trinidad and Tobago[2]
			Venezuela[2]

[1] Defined by the World Health Organization as countries or areas where YF "has been reported currently or in the past and vectors and animal reservoirs currently exist." See current Annex

Table 4-27. Countries that require proof of yellow fever (YF) vaccination from all arriving travelers[1]

Angola	Guinea-Bissau
Burundi	Mali
Cameroon	Niger
Central African Republic	Nigeria
Chad	Sierra Leone
Congo, Repubic of the	South Sudan
Côte d'Ivoire	Togo
Democratic Republic of Congo	Uganda
Gabon	
Ghana	

Illnesses in returned travelers

- Up to 64% of international travelers returning to US self-report an illness related to their travel
  - Only 8% see a physician
- Most frequently reported illness categories in GeoSentinel surveillance network study from US clinic sites 1997-2011:
  - Acute diarrhea: 22%
  - Other GI: 15%
  - Febrile/systemic illness: 14%
    - Malaria, viral syndrome, dengue, EBV
  - Dermatologic: 12%
  - Chronic diarrhea: 8%
  - Respiratory: 8%
  - Nonspecific: 5%

Harvey MMWR 2013;63:1-23.

Fever in returned travelers

- Most serious illness in returned travelers
- May not be febrile at time of presentation
- Febrile patients more likely to need hospitalization, particularly if elderly
- Multidrug resistant organisms present and increasing globally, other infection control concerns
- Malaria is most common specific diagnosis and most common cause of death in febrile travelers
  - Fever in a traveler to a malaria endemic area is a medical emergency!

Wilson Clin Infect Dis 2007;44:1560-8.

Formulating a differential in a febrile traveler

- Location(s) of travel
  - Epidemiology of infectious diseases
- Dates of travel
  - Incubation period
- Associated symptoms

Specific diagnoses for systemic febrile illness

Table 3. Etiologic Diagnoses within Selected Syndrome Groups, According to Travel Region.*

Syndrome and Cause	All Regions	Caribbean	Central America	South America	Sub-Saharan Africa	South Central Asia	Southeast Asia	Other or Multiple Regions†
	number of cases per 1000 patients with syndrome							
Systemic febrile illness (n=3907)								
Specific pathogen or cause reported‡	594	459	527	446	718	522	547	454
Malaria‡	352	65	133	133	622	139	130	234
Dengue‡	104	238	123	138	7	142	315	35
Mononucleosis (due to Epstein–Barr virus or cytomegalovirus)‡	32	70	69	79	10	17	32	63
Rickettsial infection‡	31	0	0	0	56	10	16	24
Salmonella typhi or *S. paratyphi* infection‡	29	22	25	17	7	141	26	24
No specific cause reported‡	406	541	473	554	282	478	453	546

Freeman NEJM 2006;354:119-30.

Febrile illnesses with global distribution

- Urinary tract infections
- Respiratory infections
  - Bacterial pneumonia
  - Tuberculosis
  - Influenza (season is year round in the tropics)
  - Other respiratory viruses
- Hepatitis A, B, C, E
- Sexually transmitted diseases (HIV, HSV)
- CMV, EBV
- Measles
- Meningococcus (higher rates in meningitis belt of Africa)
- Histoplasmosis and other fungal infections
- Toxoplasmosis (although higher rates in parts of world- Brazil)
- Legionellosis

Common infections by incubation period

Table 5-03. Common infections, by incubation period

DISEASE	USUAL INCUBATION PERIOD (RANGE)	DISTRIBUTION
Incubation <14 days		
Chikungunya	2–4 days (1–14 days)	Tropics, subtropics
Dengue	4–8 days (3–14 days)	Topics, subtropics
Encephalitis, arboviral (Japanese encephalitis, tickborne encephalitis, West Nile virus, other)	3–14 days (1–20 days)	Specific agents vary by region
Enteric fever	7–18 days (3–60 days)	Especially in Indian subcontinent
Acute HIV	10–28 days (10 days to 6 weeks)	Worldwide
Influenza	1–3 days	Worldwide, can also be acquired while traveling
Legionellosis	5–6 days (2–10 days)	Widespread
Leptospirosis	7–12 days (2–26 days)	Widespread, most common in tropical areas
Malaria, *Plasmodium falciparum*	6–30 days (98% onset within 3 months of travel)	Tropics, subtropics
Malaria, *P. vivax*	8 days to 12 months (almost half have onset >30 days after completion of travel)	Widespread in tropics and subtropics
Spotted-fever rickettsiae	Few days to 2–3 weeks	Causative species vary by region
Zika virus infection	3–14 days	Widespread in Latin America, endemic through much of Africa, Southeast Asia, and Pacific Islands

CDC Yellow book

Common illnesses by incubation period, cont.

Incubation 14 Days to 6 Weeks		
Encephalitis, arboviral; enteric fever; acute HIV; leptospirosis; malaria	See above incubation periods for relevant diseases	See above distribution for relevant diseases
Amebic liver abscess	Weeks to months	Most common in resource-poor countries
Hepatitis A	28–30 days (15–50 days)	Most common in resource-poor countries
Hepatitis E	26–42 days (2–9 weeks)	Widespread
Acute schistosomiasis (Katayama syndrome)	4–8 weeks	Most common in sub-Saharan Africa
Incubation >6 weeks		
Amebic liver abscess, hepatitis E, malaria, acute schistosomiasis	See above incubation periods for relevant diseases	See above distribution for relevant diseases
Hepatitis B	90 days (60–150 days)	Widespread
Leishmaniasis, visceral	2–10 months (10 days to years)	Asia, Africa, Latin America, southern Europe, and the Middle East
Tuberculosis	Primary, weeks; reactivation, years	Global distribution, rates and levels of resistance vary widely

CDC Yellow book

Febrile illnesses according to common clinical findings

Table 5-04. Common clinical findings and associated infections

COMMON CLINICAL FINDINGS	INFECTIONS TO CONSIDER AFTER TROPICAL TRAVEL
Fever and rash	Dengue, chikungunya, Zika, rickettsial infections, enteric fever (skin lesions may be sparse or absent), acute HIV infection, measles
Fever and abdominal pain	Enteric fever, amebic liver abscess
Undifferentiated fever and normal or low white blood cell count	Dengue, malaria, rickettsial infection, enteric fever, chikungunya, Zika
Fever and hemorrhage	Viral hemorrhagic fevers (dengue and others), meningococcemia, leptospirosis, rickettsial infections
Fever and arthralgia or myalgia, sometimes persistent	Chikungunya, dengue, Zika
Fever and eosinophilia	Acute schistosomiasis, drug hypersensitivity reaction, fascioliasis and other parasitic infections (rare)
Fever and pulmonary infiltrates	Common bacterial and viral pathogens, legionellosis, acute schistosomiasis, Q fever, leptospirosis
Fever and altered mental status	Cerebral malaria, viral or bacterial meningoencephalitis, African trypanosomiasis, scrub typhus
Mononucleosis syndrome	Epstein–Barr virus infection, cytomegalovirus infection, toxoplasmosis, acute HIV infection
Fever persisting >2 weeks	Malaria, enteric fever, Epstein-Barr virus infection, cytomegalovirus infection, toxoplasmosis, acute HIV infection, acute schistosomiasis, brucellosis, tuberculosis, Q fever, visceral leishmaniasis (rare)
Fever with onset >6 weeks after travel	*Plasmodium vivax* or *ovale* malaria, acute hepatitis (B, C, or E), tuberculosis, amebic liver abscess

CDC Yellow book

Initial evaluation of the febrile traveler

- Important to identify infections that are:
  - Rapidly progressive and/or potentially fatal
  - Public health concern
  - Treatable
- Approximately 25% of patients remain undiagnosed, but generally recover

Important questions to ask

- PMHx, surgeries, medications (chronic and new)
- Immunization history, especially travel vaccinations
- Travel itinerary (specific locations and dates)
- Type of accommodation
- Malaria chemoprophylaxis
  - Compliance is key- before, during, and after
- Use of bed nets and insect repellent

Important questions to ask, cont.

- Travel activities/exposures:
  - Water source
  - Food: raw meat, seafood, unpasteurized dairy, street food, uncooked fruits/vegetables
  - Insect bites
  - Freshwater activities (swimming, rafting, etc.)
  - Soil contact
  - Adventure travel (spelunking, ecotourism)
  - Animal exposures, especially bites
  - Sexual contact (19-26% of travelers report a new sexual contact during travel, <25% condom use)
  - Needle exposures: Tattoos, piercings, IVDU
  - Hospitalizations and other medical care (injections, transfusions, medical tourism, etc.)
  - Sick contacts
  - Mass gatherings (Hajj)

General laboratory evaluation

- Malaria evaluation
  - Multiple peripheral blood smears and rapid diagnostic tests (Binax)
- Complete blood count with differential (eosinophils)
- Basic metabolic panel
- Liver enzymes
- Urinalysis
- Cultures of **blood** +/- urine
- Chest Xray
- Stool evaluation if symptoms present
- Specific diagnostic assays as applicable
  - Not always reliable or readily available

Potentially fatal febrile illnesses in travelers

- Influenza
- Malaria
- Dengue fever
- Typhoid (enteric) fever
- Rickettsial infections
- Leptospirosis
- Many rarer causes
  - Viral hemorrhagic fevers
  - Yellow fever
  - Anthrax
  - Plague
  - Melioidosis
  - Bartonella (Oroya fever)

Empiric treatment

- Malaria
  - Artemisinin-based combination therapies
- Typhoid
  - Ceftriaxone
- Rickettsial disease
  - Doxycycline
- Leptospirosis
  - Doxycycline
- Travelers diarrhea?
  - Fever with diarrhea is an indication to treat (also bloody diarrhea)
  - Azithromycin preferred due to resistance concerns, least likely to increase risk of Hemolytic Uremic Syndrome
- Routine infections (pneumonia, UTI, cellulitis, etc.)

Febrile illnesses of public health concern

- Viral hemorrhagic fevers
  - Ebola and others (Marburg, Lassa, Crimean-Congo hemorrhagic fever)
- Severe acute respiratory infections
  - Influenza
  - MERS-CoV
  - SARS
  - COVID-19
- Measles
- Varicella
- Monkeypox
- Pulmonary tuberculosis
- Meningococcal meningitis

Summary

- Travel contributes to the global spread of infectious diseases
- Travelers should be seen in an International Travel Medicine clinic
  - Pre travel counseling
  - Post travel illness management

Questions?

- Megan.Shaughnessy@hcmed.org
- www.hcmed.org/clinics
  - Travel Medicine

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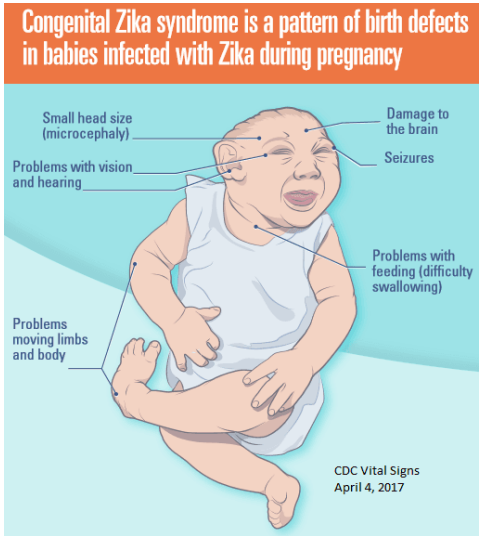
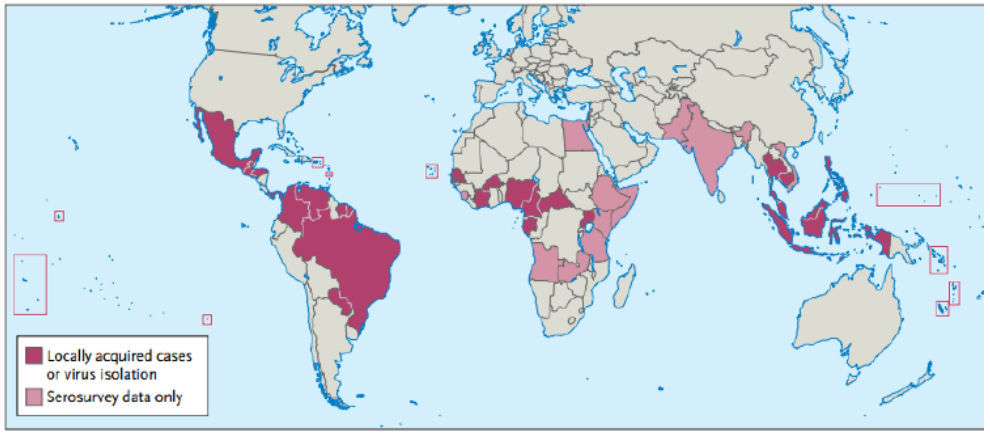
Zika



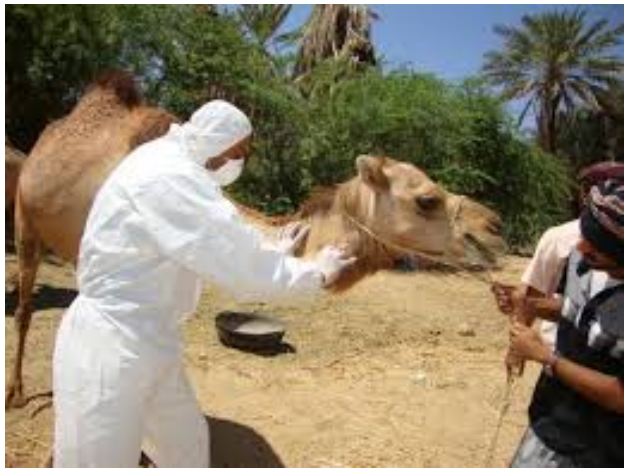
- Flavirus transmitted by Aedes mosquitoes
- 1/5 people infected symptomatic
  - Fever, conjunctivitis, rash, headache, arthralgias/myalgias
  - Incubation period 3-14 days
- Fetal malformations
- Epidemiology
  - First identified in 1947 in Uganda
  - Prior to 2007: sporadic infections in Africa and Asia
  - 2007: outbreak in Yap islands; spread throughout Pacific islands
  - 2014: spread to Central and South America
  - Miami-Dade County Florida 6-10/2016, Brownsville Texas 10-11/2016

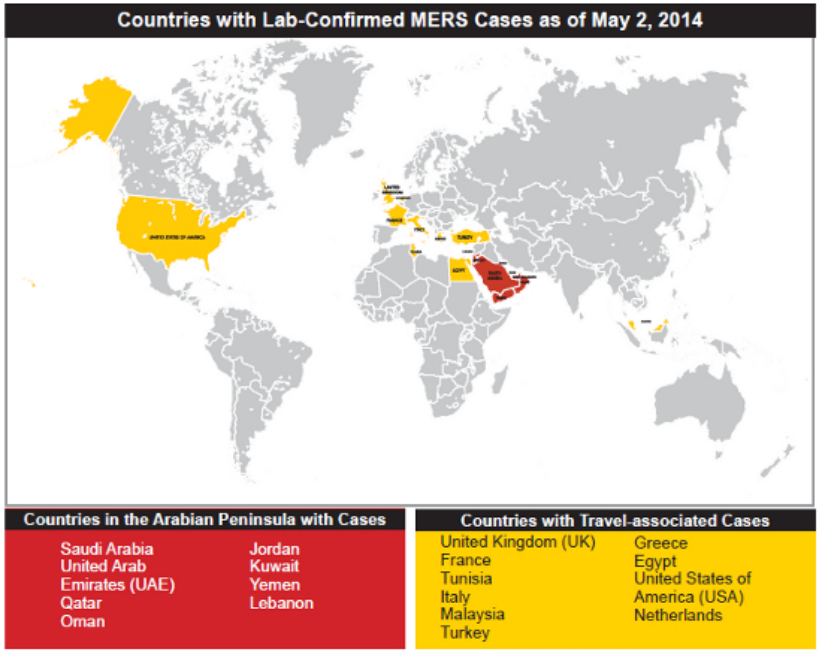


Countries with Past or Current Evidence of Zika Virus Transmission (as of December 2015).

MERS-CoV

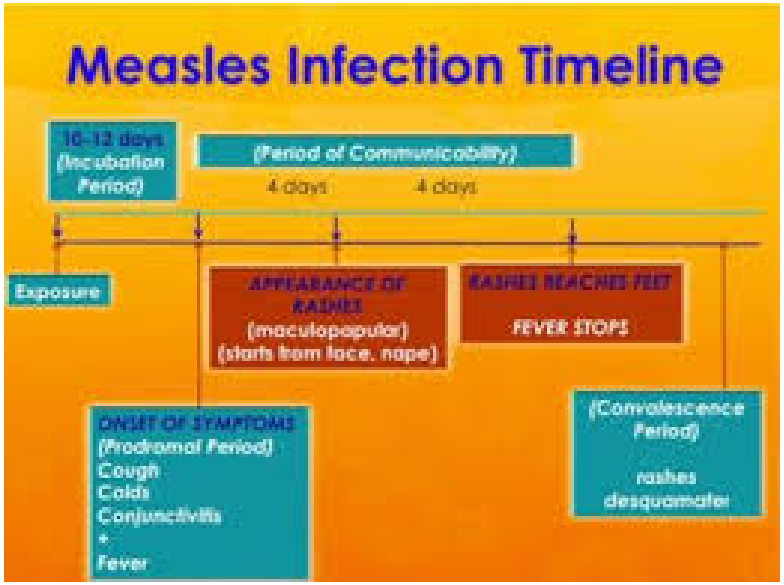
- Middle East Respiratory Syndrome, caused by a Coronavirus
  - Fever, cough, shortness of breath→ pneumonia and ARDS
- More than 2,200 cases since 2012, case fatality rate 36%
- Saudi Arabia
  - UAE, Jordan, Qatar, Oman, Kuwait, Yemen, Lebanon, Iran
- Camels: primary reservoir, spread to humans via aerosols or body fluids
- 30 imported cases, including to the US (2 cases in 2014, unrelated)
- Health care workers account for approximately 20% of cases

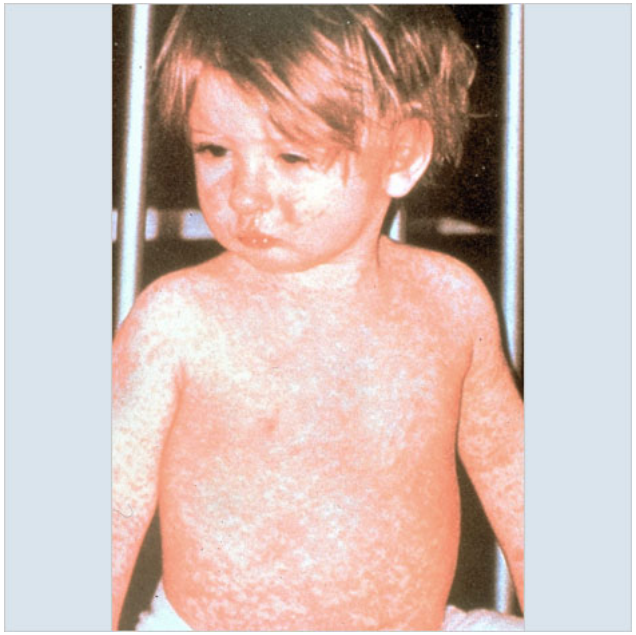




Measles virus

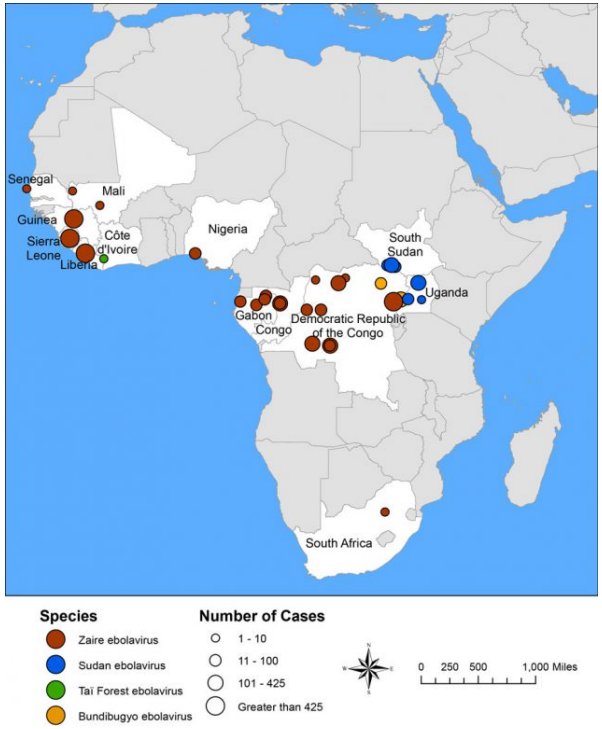
- Incubation period 7-21 days
- One of most contagious diseases
  - 90% of people susceptible and exposed → infected
- First measles vaccine introduced in US 1963
  - MMR introduced in 1971, second dose recommended 1989
- Regular outbreaks in US related to international travel and low vaccination rates
  - MN outbreaks 2011 (Somali child visiting Kenya, 21 cases) and 2017 (75 cases)
  - 2015 multistate outbreak (147 cases) originating in Disneyland
  - 2019 to date: > 700 cases, greatest number since 1994





Ebola virus

- Viral hemorrhagic fevers
  - Lassa (MN case), Marburg, Crimean-Congo hemorrhagic fever
- Direct contact with infected blood and body fluids
  - Airborne transmission “not thought to occur”
- Incubation period: 2-21 days (average 10)
- Symptoms: fever, malaise, GI, hemorrhage
  - Mortality rate 20-80%
- 2014 outbreak: largest ever at 22,000 cases
  - Originated in Guinea, spread to Liberia and Sierra Leone
  - Locally acquired cases in Spain and US
- Current outbreak in Democratic Republic of Congo, 2nd largest ever
  - Started July 2018, >1500 cases to date
  - No spread outside of DRC



MDROs

- Enterobacteriaceae:
  - Extended-spectrum Beta-lactamase (ESBL)
  - Carbapenem-resistant (CRE)
    - NDM (New Delhi Metallo-beta-lactamase)
- Salmonella typhi
- Salmonella, Shigella, Campylobacter
- Gonorrhea
- Acinetobacter
- MDR and XDR Tuberculosis

Environ Sci Technol. 2017 Dec 5;51(23):13906-13912. doi: 10.1021/acs.est.7b03380. Epub 2017 Oct 4.

Hospital Wastewater Releases of Carbapenem-Resistance Pathogens and Genes in Urban India.

Lamba M[1], Graham DW[2], Ahammad SZ[1].

India: 'Superbug' Gene Found in Environment

By **DONALD G. McNEIL Jr.** APRIL 7, 2011

Bacteria containing an antibiotic-resistant "superbug" gene have been found in 2 of 51 tap water samples in New Delhi and in dozens of puddles and pools that children could play in, according to a report published Thursday in the journal Lancet Infectious Diseases. A team from Cardiff University in Britain found the gene, NDM-1, in 11 different types of bacteria, including

Clin Infect Dis. 2015 Mar 15;60(6):837-46. doi: 10.1093/cid/ciu957. Epub 2015 Jan 21.

Antimicrobials increase travelers' risk of colonization by extended-spectrum betalactamase-producing Enterobacteriaceae.

Kantele A[1], Lääveri T[2], Mero S[3], Vilkman K[4], Pakkanen SH[5], Ollgren J[6], Antikainen J[3], Kirveskari J[3].

WHO: XDR typhoid outbreak in Pakistan tops 5,200 cases

Experts brace for more super-resistant gonorrhea

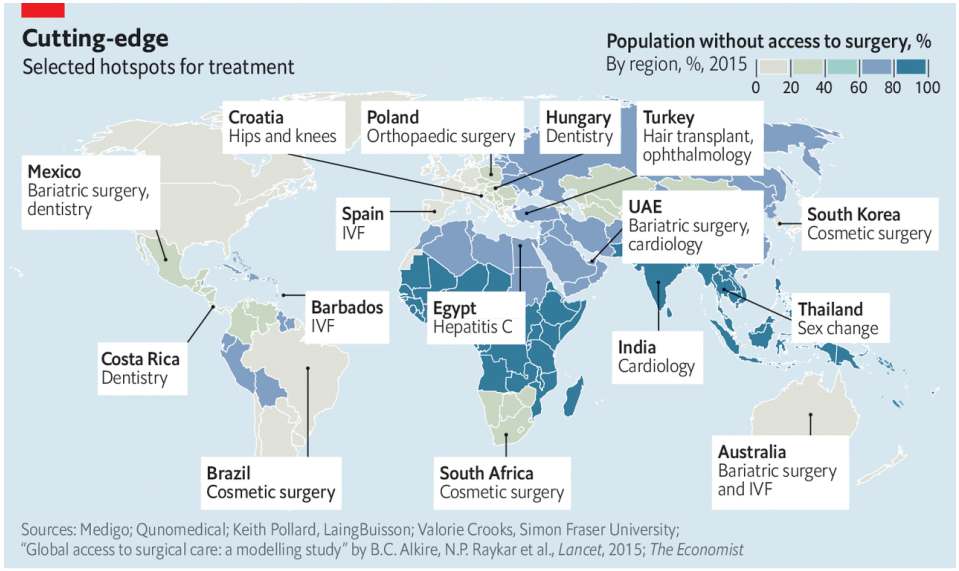
Passenger with XDR-TB dies on 3-hour flight from Turkey to Germany

An der Heiden M, et al. *Euro Surveill.* 2017;doi:10.2807/1560-7917.ES.2017.22.12.30493.

March 29, 2017

Medical tourism

- Traveling to another country for medical care
  - Cheaper
  - Immigrant returning to home country
  - Procedure not available in US
- Hundreds of thousands of US residents yearly
- Common locations: Thailand, Mexico, Singapore, India, Malaysia, Cuba, Brazil, Argentina, and Costa Rica
- Common procedures
  - Cosmetic surgery
  - Dentistry
  - Cardiac surgery
  - Others: transplant, joint replacements, oncology care, IVF
- Challenges/risks
  - Infection control: MDROs, nontuberculous mycobacteria, etc.
  - Communication issues
  - Counterfeit, poor quality, and/or expired medications
  - Flying after a procedure (blood clots)



The Economist

Diagnoses according to travel region (developing world)

Table 2. Diagnosis According to Syndrome Group and Travel Region among Ill Travelers Returning from the Developing World.*

Diagnosis	All Regions (N=17,353)	Caribbean (N=1115)	Central America (N=1326)	South America (N=1675)	Sub-Saharan Africa (N=4524)	South Central Asia (N=2403)	Southeast Asia (N=2793)	Other or Multiple Regions (N=3517)†
	number of cases per 1000 patients							
Systemic febrile illness‡	226	166	153	143	371	171	248	145
Acute diarrhea‡	222	196	234	219	167	327	210	238
Dermatologic disorder‡	170	261	225	264	127	130	212	125
Chronic diarrhea‡	113	132	173	130	57	129	97	149
Nondiarrheal gastrointestinal disorder‡	82	87	75	82	70	74	58	121
Respiratory disorder‡	77	45	49	50	77	89	97	86
Nonspecific symptoms or signs‡	70	53	51	59	75	85	63	77
Genitourinary disorder‡	35	29	11	27	51	25	29	40
Asymptomatic parasitic infection‡	30	15	26	33	29	44	30	24
Underlying chronic disease‡	19	14	23	18	20	14	13	27
Injury‡	14	23	11	14	7	15	14	21
Neurologic disorder‡	15	23	24	16	10	15	10	16
Adverse drug or vaccine reaction‡	12	4	5	5	26	12	8	8
Psychological disorder‡	12	8	20	15	8	12	10	18
Tissue parasite‡	10	5	5	11	22	4	3	7
Cardiovascular disorder	8	12	7	5	8	7	5	10
Obstetrical or gynecologic disorder	3	3	2	2	4	3	3	3
Ophthalmologic disorder	2	2	2	2	2	1	1	2
Dental problem	1	1	1	1	1	0	2	1
Death	1	1	0	0	1	3	0	1
Loss to follow-up‡	8	9	12	9	8	5	4	13

* Diagnoses included in each syndrome category are listed in the Supplementary Appendix. Numbers may not total 1000 because patients may have had more than one diagnosis.
† This category includes travel to West Asia, Northeast Asia, eastern Europe, Oceania, North Africa, or Antarctica (1868 travelers) or to multiple developing regions, for which ascertainment of exposure was impossible (1649 travelers).
‡ P<0.01 for the comparison among regions.

Freeman NEJM 2006;354:119-30.

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Neurologic disorder‡	15	23	24	16	10	15	10	16
Adverse drug or vaccine reaction‡	12	4	5	5	26	12	8	8
Psychological disorder‡	12	8	20	15	8	12	10	18
Tissue parasite‡	10	5	5	11	22	4	3	7
Cardiovascular disorder	8	12	7	5	8	7	5	10
Obstetrical or gynecologic disorder	3	3	2	2	4	3	3	3
Ophthalmologic disorder	2	2	2	2	2	1	1	2
Dental problem	1	1	1	1	1	0	2	1
Death	1	1	0	0	1	3	0	1
Loss to follow-up‡	8	9	12	9	8	5	4	13

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Freeman NEJM 2006;354:119-30.

Common illnesses by travel site

Table 5-02. Common causes of fever, by geographic area

GEOGRAPHIC AREA	COMMON TROPICAL DISEASE CAUSING FEVER	OTHER INFECTIONS CAUSING OUTBREAKS OR CLUSTERS IN TRAVELERS
Caribbean	Chikungunya, dengue, malaria (Haiti), Zika	Acute histoplasmosis, leptospirosis
Central America	Chikungunya, dengue, malaria (primarily *Plasmodium vivax*), Zika	Leptospirosis, histoplasmosis, coccidioidomycosis
South America	Chikungunya, dengue, malaria (primarily *P. vivax*), Zika	Bartonellosis, leptospirosis, enteric fever, histoplasmosis
South-central Asia	Dengue, enteric fever, malaria (primarily non-falciparum)	Chikungunya Rickettsial infections
Southeast Asia	Dengue, malaria (primarily non-falciparum)	Chikungunya, leptospirosis
Sub-Saharan Africa	Malaria (primarily *P. falciparum*), tickborne rickettsiae (main cause of fever in southern Africa), acute schistosomiasis, dengue	African trypanosomiasis, chikungunya, enteric fever, filariasis

CDC Yellow book

GeoSentinel Surveillance Network

Established in 1995, maintained by CDC

54 clinics sites, 235 network members

- HealthPartners Center for International Health, Regions Hospital, St Paul

26 countries, 6 continents

Collects demographic, travel, and clinical diagnosis surveillance data from ill international travelers

Rapid messaging system between all sites and network members

FIGURE 1. Locations of GeoSentinel surveillance sites* and network members†

* N = 54.
† N = 235.

Harvey MMWR 2013;63:1-23.

Persistent diarrhea

- Diarrhea > 2 weeks:
- Most common etiology from GeoSentinel study:
  - Postinfectious irritable bowel syndrome 55%
  - Unknown 32%
  - Irritable bowel syndrome 4%
  - Ulcerative colitis 3%
  - Postinfectious lactose intolerance 1%
- Often not infectious!
  - Exception- protozoan pathogens
    - *Giardia* most common, upper GI symptoms predominate
  - Rare exception- bacterial pathogens
    - Children with enteroaggregative or enteropathogenic *E. coli*
    - *C. difficile*

Harvey MMWR 2013;63:1-23.