

# Travel Medicine 2015



[themindfulword.org](http://themindfulword.org)

**David Fessler, MD, MPH**

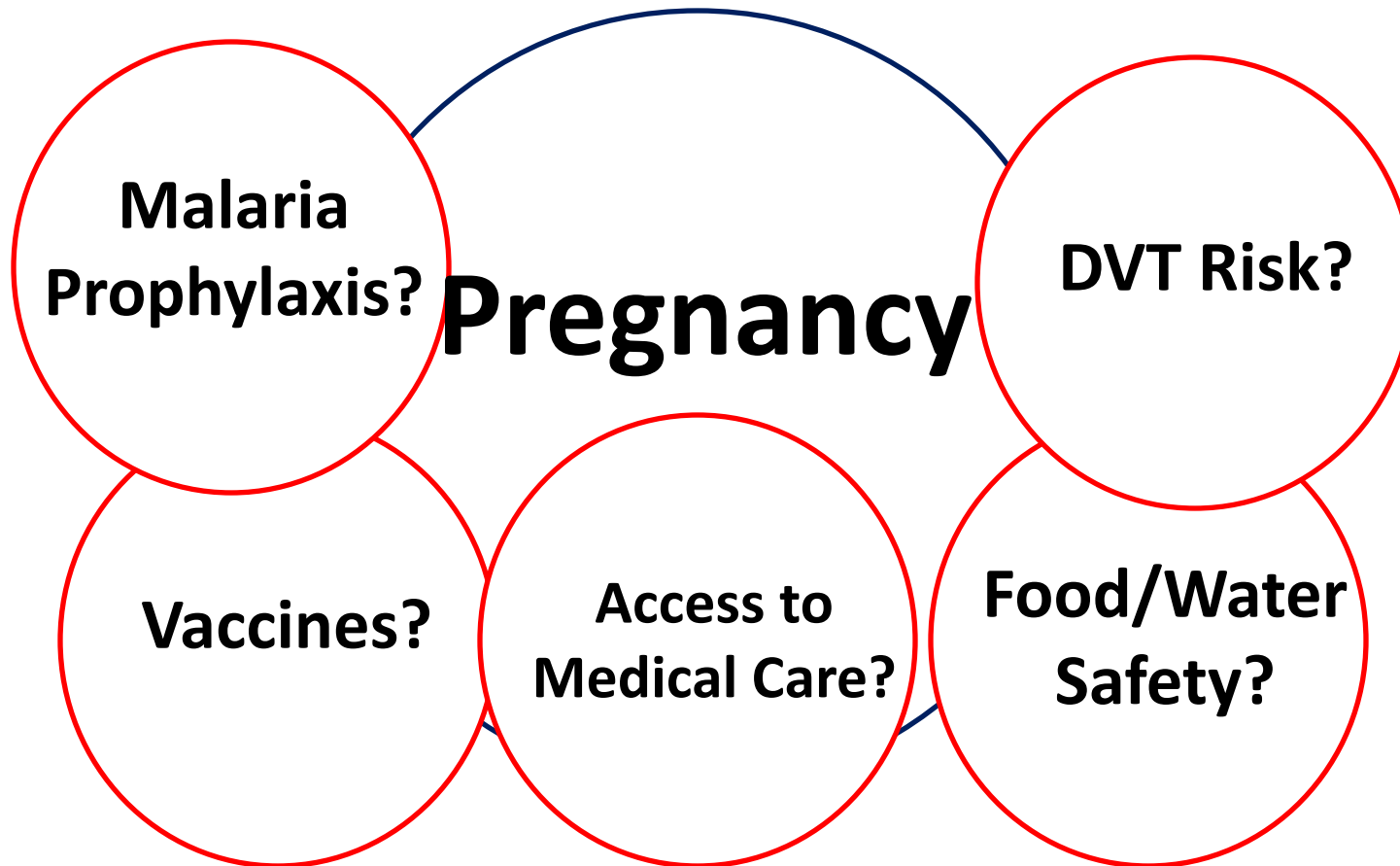
Division of General Medicine and Primary Care

Division of Infectious Diseases

Beth Israel Deaconess Medical Center

## Phone message:

*Patient leaving for Nigeria next month for 3 weeks to see family. 10 weeks pregnant. Requesting valium for flight. Please advise.*



# Online Resources for Travel Health

## CDC Traveler's Health

<http://www.cdc.gov/travel/>



## WHO International Traveler and Health

<http://www.who.int/ith/en/>



World Health Organization

## State Department Travel Advisories

<http://travel.state.com>



## Paid subscription online services

- Up-to-Date
- Travax.com

A 24 year old woman books an urgent care visit with you. She has been experiencing 3 days of high fever to 103.5F. Yesterday, she started a faint, lacy rash over her torso and this morning developed pain and swelling in her wrists and ankles. She returned from a weeklong trip to St. Thomas a week ago.

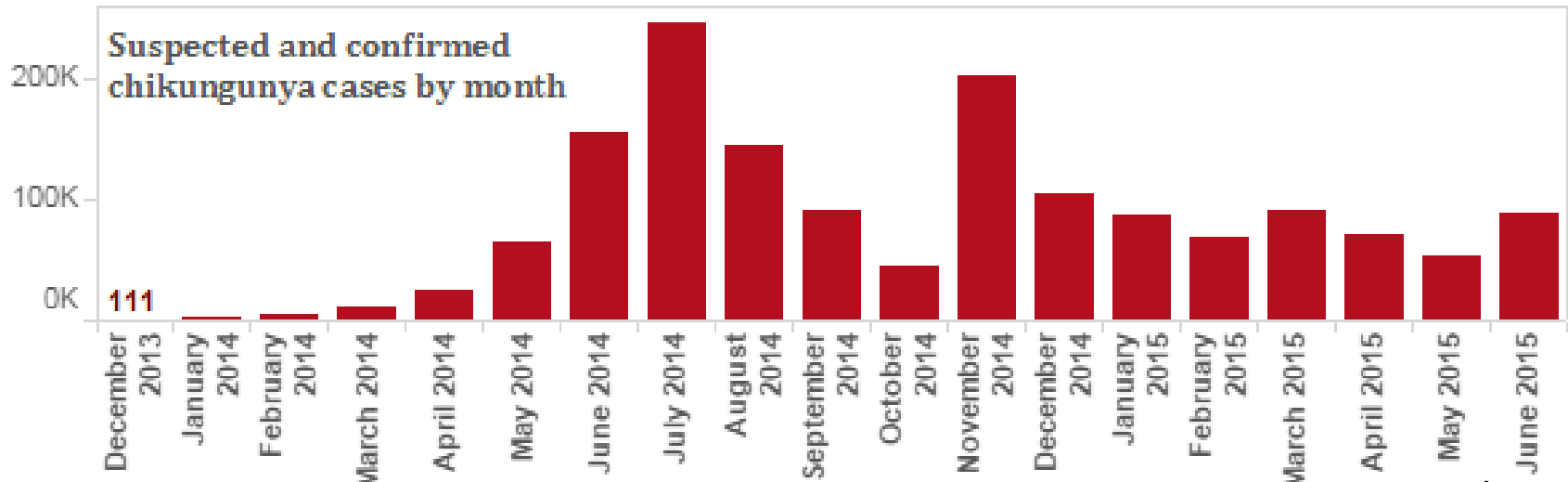
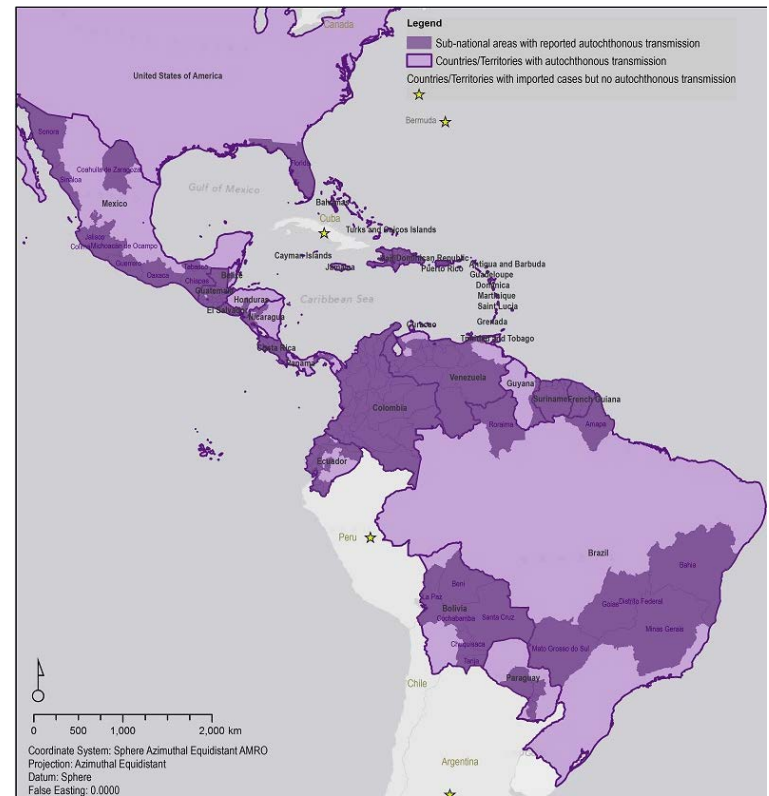
- What could this patient have done to reduce the risk of acquiring this infection?
- What would you advise her about prognosis and treatment?



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# Lindsay Lohan Reveals She Has Chikungunya: Rare, Untreatable Virus

Wed, December 31, 2014 9:01am EDT by Lauren Cox 8 Comments





# Preventing Mosquito Bites

## Physical protection

- Limit exposure to standing water
- Long sleeved shirt, long pants, socks, wide brim hat
- Light-colored clothing
- Screened and/or air conditioned rooms
- Permethrin-impregnated bed nets

## Insect Repellents

- DEET (10-35% for casual exposures, 35-50% for intense exposures, or high heat/humidity)
- Icaridin, PMD (lemon eucalyptus oil)
- Permethrin-treated clothing
- Area repellents (mosquito coils, aerosolizers, etc)



[guardian.co.uk](http://guardian.co.uk)

# Chikungunya

## **Natural History:**

Fevers last 3-5 days

- Joint symptoms persist in ~80% of patients
- Arthralgias or inflammatory arthritis, tenosynovitis
- Mean duration: 6 months in some studies

## **Treatment:**

Supportive care: NSAIDs, Tylenol

No antiviral treatments found to be effective

No established treatments for prolonged joint symptoms

Small cases series have described efficacy with DMARDs for those with persistent inflammatory arthritis

- Hydroxychloroquine
- Methotrexate
- Corticosteroids

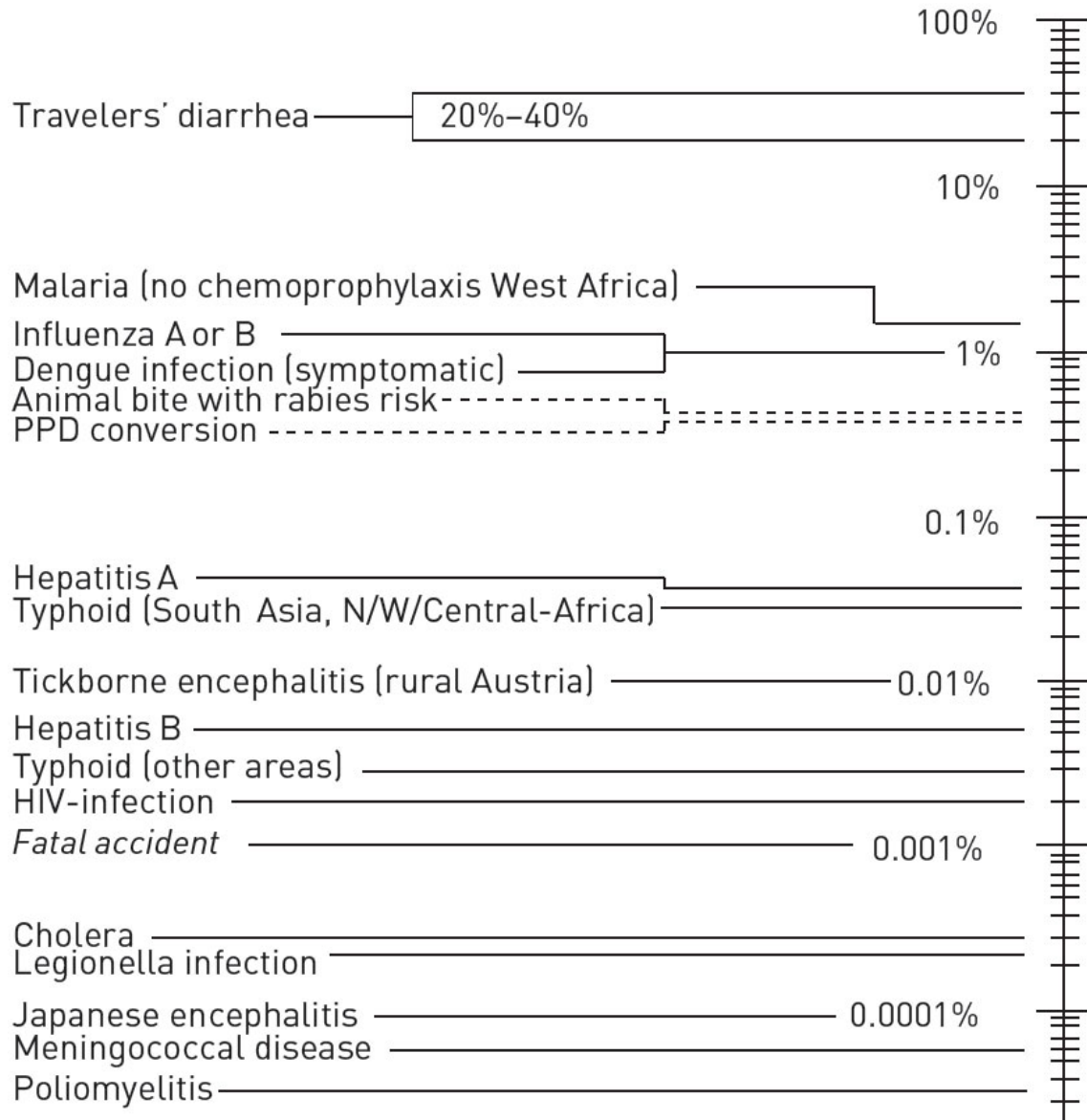
# Causes of Fever in the Returning Traveler: Location, Location, Location

- Retrospective study of 17,353 travelers presenting to GeoSentinel clinics at 30 sites on 6 continents 1996-2004
- Looked at travelers returning from 6 regions of developing world
- Most frequent causes of fever (per 1000):

	Global	Caribbean	Central America	South America	Sub-Saharan Africa	South-Central Asia	Southeast Asia
<b>Malaria</b>	352	65	133	133	622	139	130
<b>Dengue</b>	104	238	123	138	7	142	315
<b>Rickettsial infections</b>	31	0	0	0	56	10	16
<b>Typhoid/Paratyphoid</b>	29	22	25	17	7	141	26
<b>No cause reported</b>	406	541	473	554	282	478	453



# Estimated Incidence Per Month of Infections and Fatal Accidents Among Travelers in Developing Countries in 2010

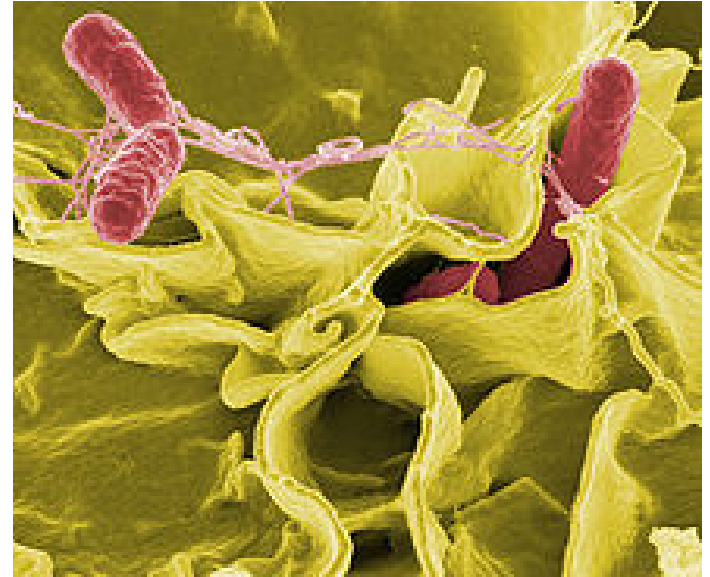


A 35 year old woman tells you at her annual visit that she is leaving tomorrow for a week-long vacation to Mexico City. She is otherwise healthy, and is confident she is not pregnant.

- 1) How would you advise this patient about behavioral steps she can take to minimize the risk of travelers' diarrhea?
- 2) What pharmacologic options would you consider for prevention or treatment of travelers' diarrhea

# Travelers' Diarrhea

- Occurs in 30-60% of travelers
  - 80-90% due to bacterial pathogens
- Most common pathogens:
  - E. coli (especially ETEC)
  - Campylobacter
  - Shigella
  - Salmonella
  - Viruses (norovirus, etc)



[en.wikipedia.org](http://en.wikipedia.org)

- Parasites relatively uncommon, but become more likely with lengthy travel or protracted symptoms
  - Giardia, Entameoba, Cyclospora, Isospora, Cryptosporidium

# Food/Water Safety

- Wash hands before eating, either with soap & water or alcohol-based gel
- Drink/brush teeth with bottled or boiled water
  - Avoid tap water, ice cubes, pre-opened water bottles
- Avoid food purchased from street vendors
- Make sure food is fully and recently cooked
- Avoid unpasteurized dairy products
- Avoid raw fruits/vegetables unless traveler peels them



parentsconnect.com



growcookeat.com



myfrenchkitchen.wordpress.com

# Prevention of Travelers' Diarrhea

## Bismuth subsalicylate (Pepto-Bismol)

- Anti-microbial, anti-secretory, and toxin absorption properties
- 40-65% protective for prevention of travelers' diarrhea
- Standard dosing: two tablets qid - inconvenient
- Side effects: Black tongue and stool
- Impairs absorption of doxycycline
- Contraindications: Pregnancy, advanced CKD, aspirin allergy
- Precautions:
  - Bleeding with use of anticoagulants
  - Risk of toxicity when used with other salicylates



# Prevention of Travelers' Diarrhea

## Probiotics

Safe, but not routinely recommended due to unclear efficacy

- Single RCT showed efficacy of daily Lactobacillus GG over placebo
  - 47% protection (3.9% vs 7.4% with diarrhea on given day)
- Another RCT with 245 travelers showed **no** protective benefit with twice daily Lactobacillus LA compared to placebo



[guardian.co.uk](http://guardian.co.uk)

Hilton, J Travel Med 1997;4:41

Briand, Clin Infect Dis 2006;43:1170

# Prevention of Travelers' Diarrhea

## Prophylactic Antibiotics

- Very efficacious (up to 90%)
- Main concerns are drug resistance and antibiotic-related toxicities
- Growing resistance has already made tetracyclines and TMP-SMX ineffective, and fluoroquinolone resistance is spreading quickly

## Rifaximin

- Intraluminal, non-absorbed rifamycin derivative
- No efficacy against invasive infections like *Campylobacter* or *Shigella*
- FDA approved for treatment (**not prevention**) of travelers diarrhea
- Meta-analysis of four RCTs showed efficacy at preventing travelers' diarrhea (RR 0.41,  $p < 0.00001$ )
- Often not covered by insurers, high out-of-pocket cost

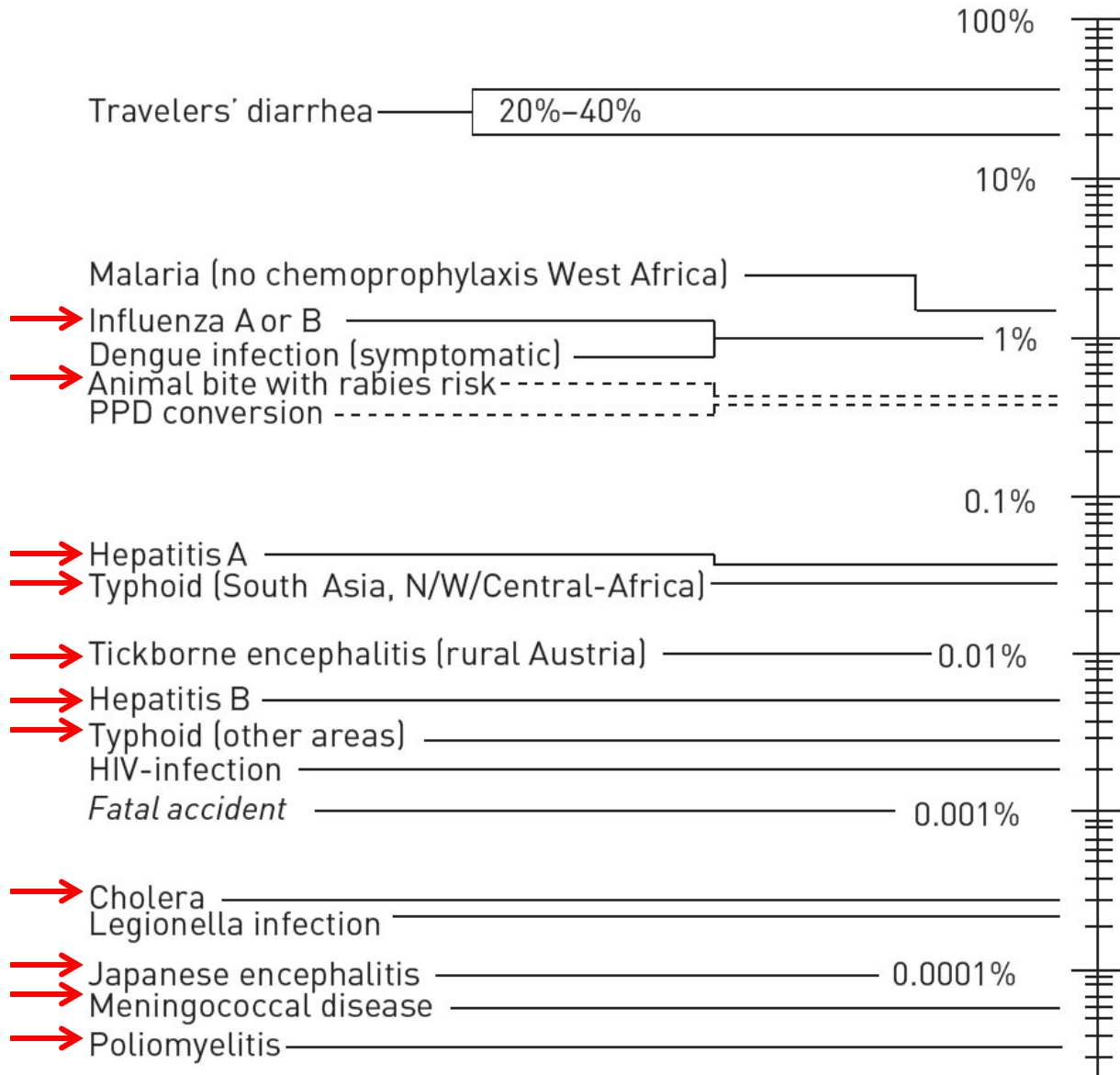


# Travelers' Diarrhea

## Early Self-Treatment

- In general, should focus on early self-treatment rather than prophylaxis, offering prophylaxis only for high risk patients
- Usually ciprofloxacin 500mg bid or levofloxacin 500mg qd x 1-3 days
- In pregnancy, or in South/Southeast Asia with high incidence of fluoroquinolone-resistant *Campylobacter*:
  - Azithromycin 500mg daily x 1-3 days
- Anti-motility agents usually safe, controversial in severe disease due to concerns about prolonged bacterial carriage
- High fevers, bloody stools, lack of resolution should prompt medical evaluation

# Estimated Incidence Per Month of Infections and Fatal Accidents Among Travelers in Developing Countries in 2010



A 45-year-old man with history of rheumatoid arthritis on infliximab sees you in clinic for a blood pressure check. Hand on the doorknob, he mentions that he is excited for his trip to India next month.” Further investigation reveals that he will be spending a week at the Hilton in Mumbai for business. Afterwards, he is flying to New Delhi and Agra to see the Taj Mahal. He leaves in 4 weeks.

- 1)** What travel-related infections is this immunocompromised patient at increased risk for?
- 2)** What routine vaccines do you want to verify this patient has received?
- 3)** What travel-specific vaccines would you consider for this patient? How does his immunocompromised status affect this decision?

# TNF $\alpha$ -blocker associated infections:

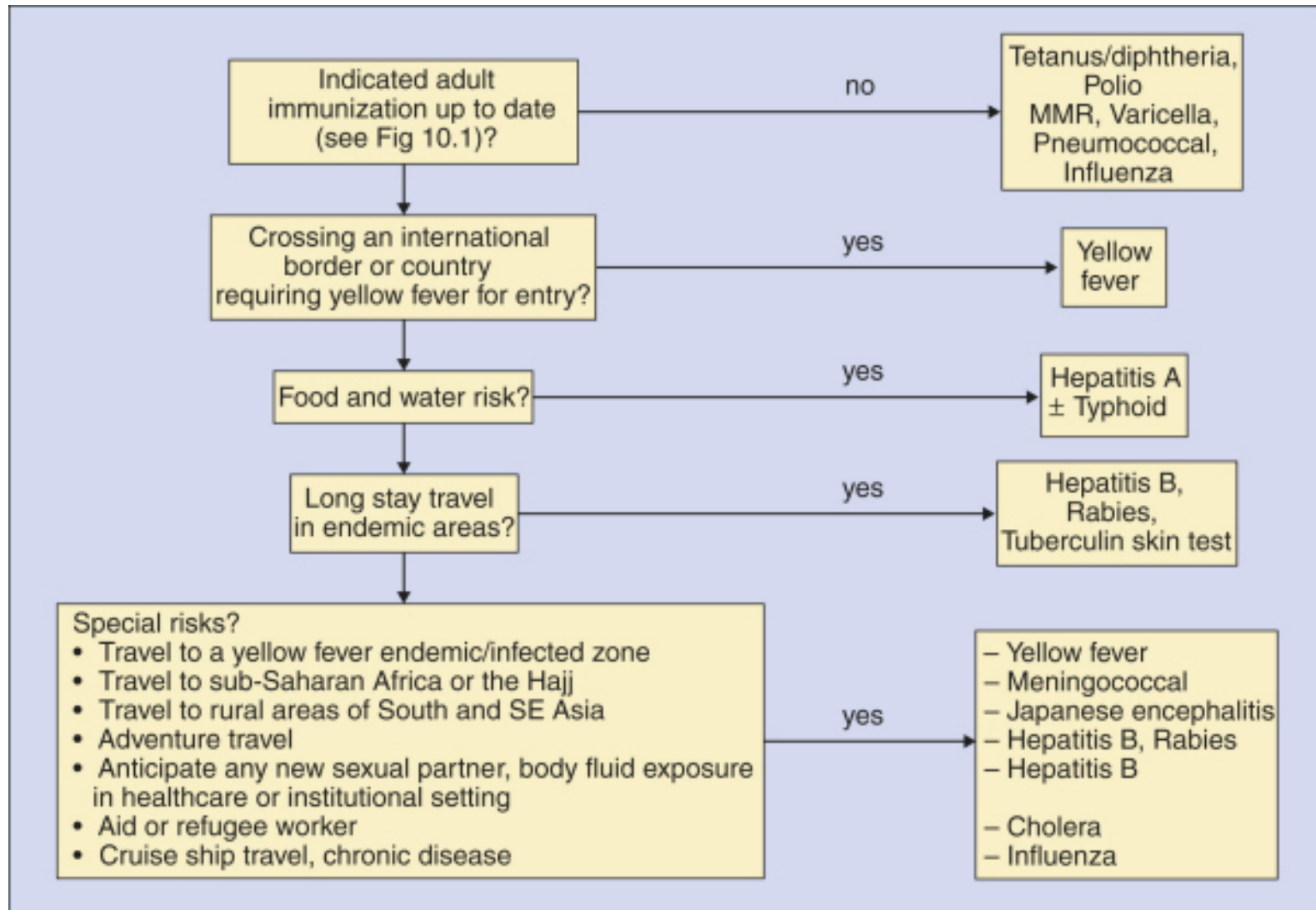
- TB
- Listeria
- Legionella
- Endemic fungi
  - Histoplasma
  - Coccidioides



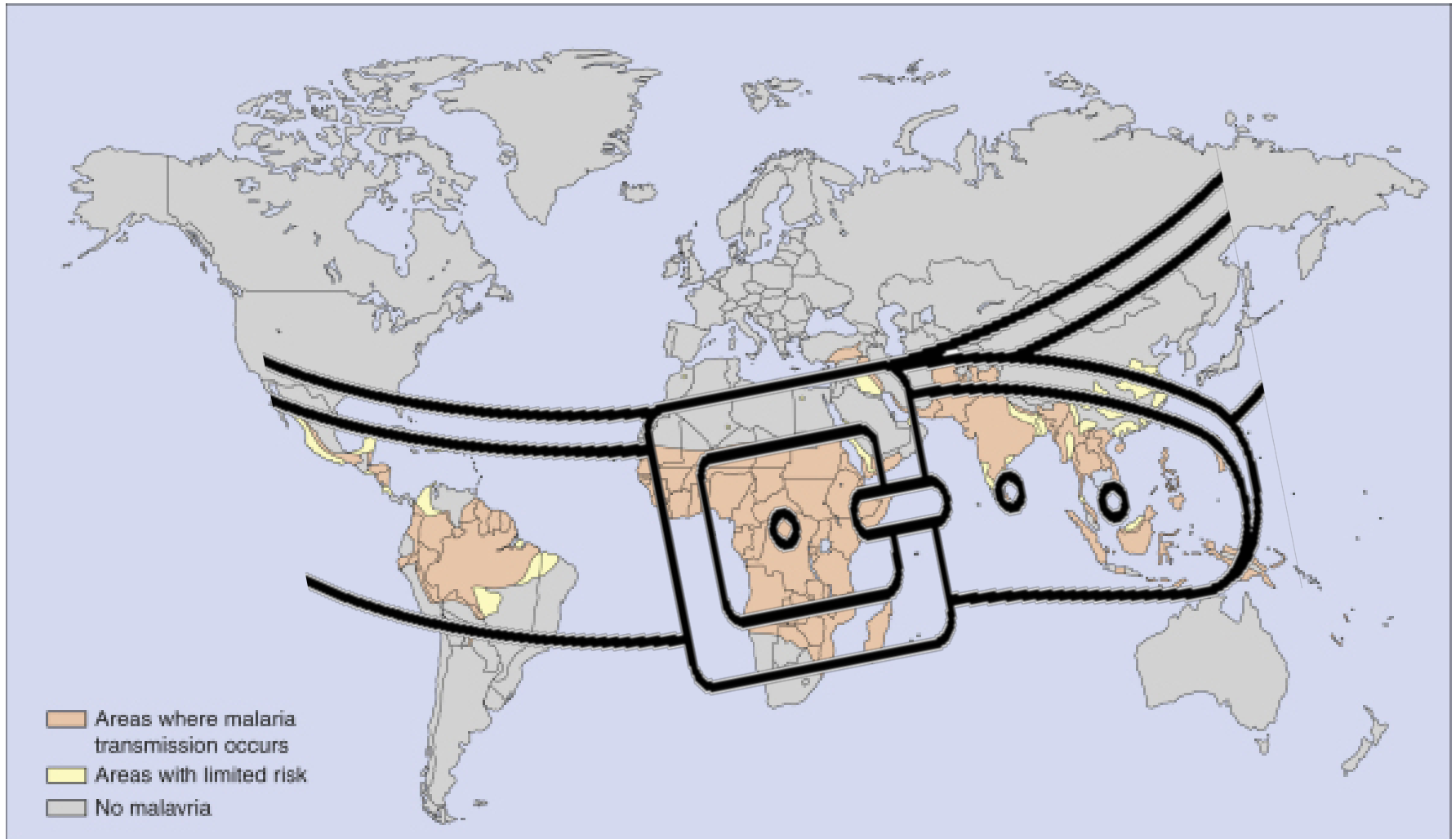
**Figure 2. Vaccines that might be indicated for adults based on medical and other indications<sup>1</sup>**

VACCINE ▼	INDICATION ►	Pregnancy	Immuno-compromising conditions (excluding human immunodeficiency virus [HIV]) <sup>4A,7A,11</sup>	HIV infection CD4+ T lymphocyte count <sup>4A,7A,11</sup>		Men who have sex with men (MSM)	Kidney failure, end-stage renal disease, receipt of hemodialysis	Heart disease, chronic lung disease, chronic alcoholism	Asplenia (including elective splenectomy and persistent complement component deficiencies) <sup>4,12</sup>	Chronic liver disease
				< 200 cells/μL	≥ 200 cells/μL					
Influenza <sup>7,2</sup>			1 dose IIV annually			1 dose IIV or LAIV annually	1 dose IIV annually			
Tetanus, diphtheria, pertussis (Td/Tdap) <sup>7,2</sup>	1 dose Tdap each pregnancy		Substitute 1-time dose of Tdap for Td booster; then boost with Td every 10 yrs							
Varicella <sup>7,4</sup>		Contraindicated			2 doses					
Human papillomavirus (HPV) Female <sup>7,2</sup>		3 doses through age 26 yrs			3 doses through age 26 yrs					
Human papillomavirus (HPV) Male <sup>7,2</sup>		3 doses through age 26 yrs			3 doses through age 21 yrs					
Zoster <sup>4</sup>		Contraindicated			1 dose					
Measles, mumps, rubella (MMR) <sup>7,2</sup>		Contraindicated			1 or 2 doses					
Pneumococcal 13-valent conjugate (PCV13) <sup>7,8</sup>					1 dose					
Pneumococcal polysaccharide (PPSV23) <sup>4</sup>					1 or 2 doses					
Meningococcal <sup>7,9</sup>					1 or more doses					
Hepatitis A <sup>7,10</sup>					2 doses					
Hepatitis B <sup>7,11</sup>					3 doses					

# Pre-Travel Immunizations



# Malaria Prevention



Schlagenhauf-Lawlor P, Kain KC. 2008. Malaria Chemoprophylaxis, in Keystone JS, Kozarsky PE, Freedman DO, Northdurft HD, Commor BA, ed. *Travel Medicine, 2<sup>nd</sup> ed.*, Mosby Elsevier, p.139.



# Malaria Chemoprophylaxis

**19F traveling to Haiti for 2 weeks for service work.**

- No medical issues or allergies, not pregnant.

**42M moving to Namibia for a year for missionary work**

- History of hypertension, no drug allergies

**28F, 24 weeks pregnant, traveling to Nigeria to see family.**

- No other medical issues, no drug allergies

## Chemoprophylaxis options

- a) Chloroquine
- b) Mefloquine (Lariam)
- c) Atovaquone/proguanil (Malarone)
- d) Doxycycline
- e) Other

# Malaria in the United States

TABLE 1. Number of malaria cases\* among U.S. military personnel and U.S. and foreign civilians — United States, 1970-2012

Year	U.S. military personnel	U.S. civilians	Foreign residents	Status not recorded	Total	Area or region	No.	(%)
2007	33	701	263	508	1,505	Africa	1151	(77.3)
2008	19	510	176	593	1,298	Asia	183	(12.2)
2009	18	661	201	604	1,484	Central America/ Caribbean	64	(4.3)
2010	46	1,085	368	192	1,691	South America	37	(2.5)
2011	91	1,098	386	350	1,925	Oceania	7	(0.5)
2012	43	1,121	328	195	1,687	Unknown	47	(3.2)
						<b>Total</b>	<b>1,489</b>	<b>(100)</b>

<i>Plasmodium</i> species	2012		Category	No.	(%)
	No.	(%)			
<i>P. falciparum</i>	985	(58.4)	Visiting friends and relatives	603	(53.9)
<i>P. vivax</i>	280	(16.6)	Tourist	32	(2.9)
<i>P. malariae</i>	54	(3.2)	Missionary or dependent	80	(7.2)
<i>P. ovale</i>	59	(3.5)	Business representative	92	(8.2)
<i>P. knowlesi</i>	0	(0)	Student or teacher	47	(4.2)
Mixed	21	(1.2)	Air crew or sailor	4	(0.4)
Undetermined	288	(17.1)	Other	6	(0.5)
<b>Total</b>	<b>1,687</b>	<b>(100)</b>	Unknown	44	(3.9)
				210	(18.8)

# Malaria Chemoprophylaxis

## Chloroquine

Widespread resistance, but still agent of choice in sensitive areas

- Haiti, DR, Caribbean, parts of Central America, most of Middle East

### Dosing:

Weekly, starting 1-2 weeks before departure, and continuing for 4 weeks after return

### Adverse effects:

- Uncommon: GI intolerability, neuropsychiatric symptoms, pruritis in dark-skinned people
- Keratopathy, retinopathy reported in long-term use

### Contraindications/precautions:

- G6PD deficiency, pre-existing retinopathy or CNS diseases
- May exacerbated porphyria or psoriasis

# Malaria Chemoprophylaxis

## **Mefloquine (Lariam):**

Drug resistance rare, except along Thai-Cambodian and Thai-Burmese borders

## **Dosing:**

Weekly, start 1-2 weeks before, continue 4 weeks after return

## **Neuropsychiatric side effects:**

Wide variability in reported incidence and severity

- Well-tolerated vivid dreams: up to 25%
- Nightmares, insomnia, depression: 1/200 to 1/600
- Seizures, psychosis, encephalopathy: 1/6,000 to 1/10,000

## **Precautions/Contraindications:**

Significant psychiatric disease, seizure disorder

# Malaria Chemoprophylaxis

## **Atovaquone/Proguanil (Malarone):**

- Only sporadic reports of drug resistance
- Cost considerations aside, used by many as agent of choice in chloroquine-resistant areas

## **Dosing:**

- Daily, start 1 day before departure and continue 7 days after return

## **Adverse effects:**

- Very well tolerated. Rare GI side effects

## **Precautions/Contraindications:**

- Renal insufficiency (GFR < 30)
- Pregnancy class C due to lack of safety data for atovaquone

# Malaria Chemoprophylaxis

## **Doxycycline**

- No reports of drug resistance
- Useful in those traveling to chloroquine-resistant areas who can't tolerate mefloquine or afford atovaquone/proguanil

## **Dosing:**

- Daily, start 1 day before departure, continue 4 weeks after return

## **Adverse effects:**

- GI side effects, phototoxicity

## **Precautions/Contraindications:**

- Pregnancy, breast feeding, children under 8

# Malaria Chemoprophylaxis in Pregnancy

Pregnant travelers should generally avoid travel to malarious areas

- Increased risk of severe malaria, increased maternal and fetal death
- Sequestration of parasites in placenta, with IUGR, premature delivery, anemia, congenital malaria
- If travel unavoidable, personal protection measures are critical
- DEET thought to be safe, though limited data in 1<sup>st</sup> trimester

## **Chemoprophylaxis:**

- Chloroquine safe in sensitive areas
- Mefloquine only option in chloroquine-resistant areas
  - Safety data exists during 2<sup>nd</sup> and 3<sup>rd</sup> trimester, but limited data in 1<sup>st</sup> trimester



# Malaria Chemoprophylaxis Cases

19F traveling to Haiti for 2 weeks for service work.

- No medical issues or allergies, not pregnant.

**Anything, including Chloroquine**

42M moving to Namibia for a year for missionary work

- History of hypertension, no drug allergies

**Doxycycline, Atovaquone/proguanil (Malarone), or Mefloquine**

28F, 24weeks pregnant, traveling to Nigeria to see family.

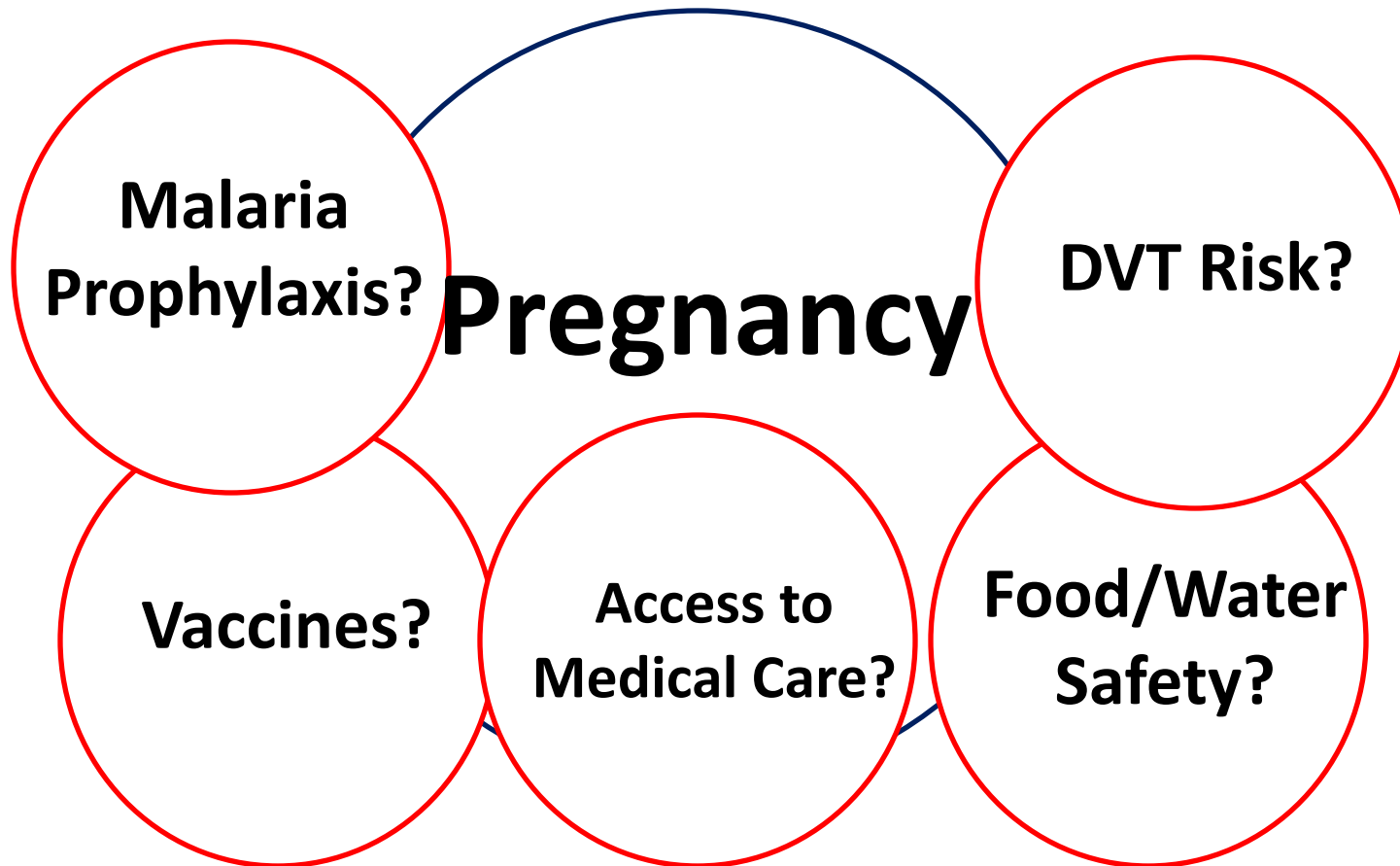
- No other medical issues, no drug allergies

**Avoid travel if at all possible. If travel unavoidable:**

**Mefloquine (Lariam)**

## Phone message:

*Patient leaving for Nigeria next month for 3 weeks to see family. 10 weeks pregnant. Requesting valium for flight. Please advise.*



## **Phone message:**

*Patient leaving for Nigeria next month for 3 weeks to see family. 10 weeks pregnant. Requesting valium for flight. Please advise.*

## **High risk scenario:**

- Malaria-endemic area with limited chemoprophylaxis options
- Yellow-fever endemic area, vaccine pregnancy class “C”
- “Visiting friends and family”
  - Potential risks for food/water borne illness
- Access to obstetric care?

Consider deferring trip if possible

If travel unavoidable:

- Mefloquine, travel vaccines (incl. YFV), lots of counseling!

# Summary

- Fever in the returning traveler: location, location, location!
- Much pre-travel preparation can happen in a primary care office
  - Hep A, Typhoid, Cipro, travel counseling, +/- malaria prophylaxis can take care of the majority of travelers
- Online, updated resources for destination-specific information
- Travel clinic preferable for those requiring Yellow Fever vaccine, pregnancy, immunosuppression



[theaustralian.com.au](http://theaustralian.com.au)



[venere.com](http://venere.com)

- Briand V et al. Absence of efficacy of nonviable *Lactobacillus acidophilus* for the prevention of travelers diarrhea: A randomized, double-blind, controlled study. *Clin Infect Dis* 2006;43(9):1170
- Centers for Disease Control and Prevention. Malaria Surveillance – United States, 2012. *MMWR* 2014;63(No 12):1
- Centers for Disease Control and Prevention. CDC Health Information for International Travel 2014. New York: Oxford University Press; 2014. <http://www.cdc.gov/travel/>
- Centers for Disease Control and Prevention. Recommended adult immunization schedule – United States, 2013. *MMWR* 2013;62(1):9
- Hargarten S et al. Overseas fatalities of United States citizen travelers: An analysis of deaths related to international travel. *Ann Emerg Med* 1991;20(6):622
- Hilton E et al. Efficacy of *Lactobacillus GG* as a diarrheal preventive in travelers. *J Travel Med* 1997;4(1):41
- Hu Y, Ren J, Zhan M, Dai H. Efficacy of rifaximin in prevention of travelers' diarrhea: a meta-analysis of randomized, double-blind, placebo-controlled trials. *J Travel Med* 2012;19:352.
- Keystone JS, Kozarsky PE, Freedman DO, Northdurft HD, Commor BA, ed. *Travel Medicine, 2<sup>nd</sup> ed.*, Mosby Elsevier.
- Martinez-Sandoval F. Prevention of travelers' diarrhea with rifaximin in US travelers to Mexico. *J Travel Med* 2010;17(2):111
- Peltola H et al. Prevention of travellers' diarrhoea by oral B-subunit/whole cell cholera vaccine. *Lancet* 1991;338:1285
- Redman CA, MacLennan A, Walker E. Causes of death abroad: Analysis of data on bodies returned for cremation to Scotland, 2000-2004. *J Travel Med* 2011;18:96.
- Scerpella EG, Sanchez JL, Matthewson JJ et al. Safety, immunogenicity, and protective efficacy of the whole cell/recombinant B subunit (WC/rBS) oral cholera vaccine against travelers' diarrhea. *J Travel Med* 1995;2:22.
- US Dept of Commerce, Office of Travel and Tourism Industries. Profile of U.S. resident travelers visiting overseas destinations: 2014 outbound. <http://tinet.ita.doc.gov>



A photograph of a herd of elephants walking away from the camera on a dirt path in a savanna. The path is reddish-brown and flanked by lush green vegetation. There are four elephants visible: a large adult on the left, a smaller calf in the middle, and another large adult on the right with a smaller calf walking beside it. The scene is brightly lit, suggesting a sunny day.

*Thank you!*