Travel Medicine

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Disclosure

- No conflict of interest to disclose

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Outline

- Epidemiology
- Pre-travel consultation
  - Risk Assessment
  - Vaccinations and Prophylaxis
  - Self-treated conditions
- Evaluation of returning traveler

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Epidemiology

- In 2015 international tourist arrivals in all countries exceeded 1.2 billion persons
  - Increasing travel to developing countries, especially Asia and sub-Saharan Africa
  - Leisure/Recreation
  - Visiting Friends/Relatives
  - Business
  - Humanitarian work/Teaching

Epidemiology

- Forty percent seek pre-travel counseling
  - Very low in those visiting friends/relatives (VFRs)
- 22-64% report illness associated w/ travel
- Up to 8% seek medical attention

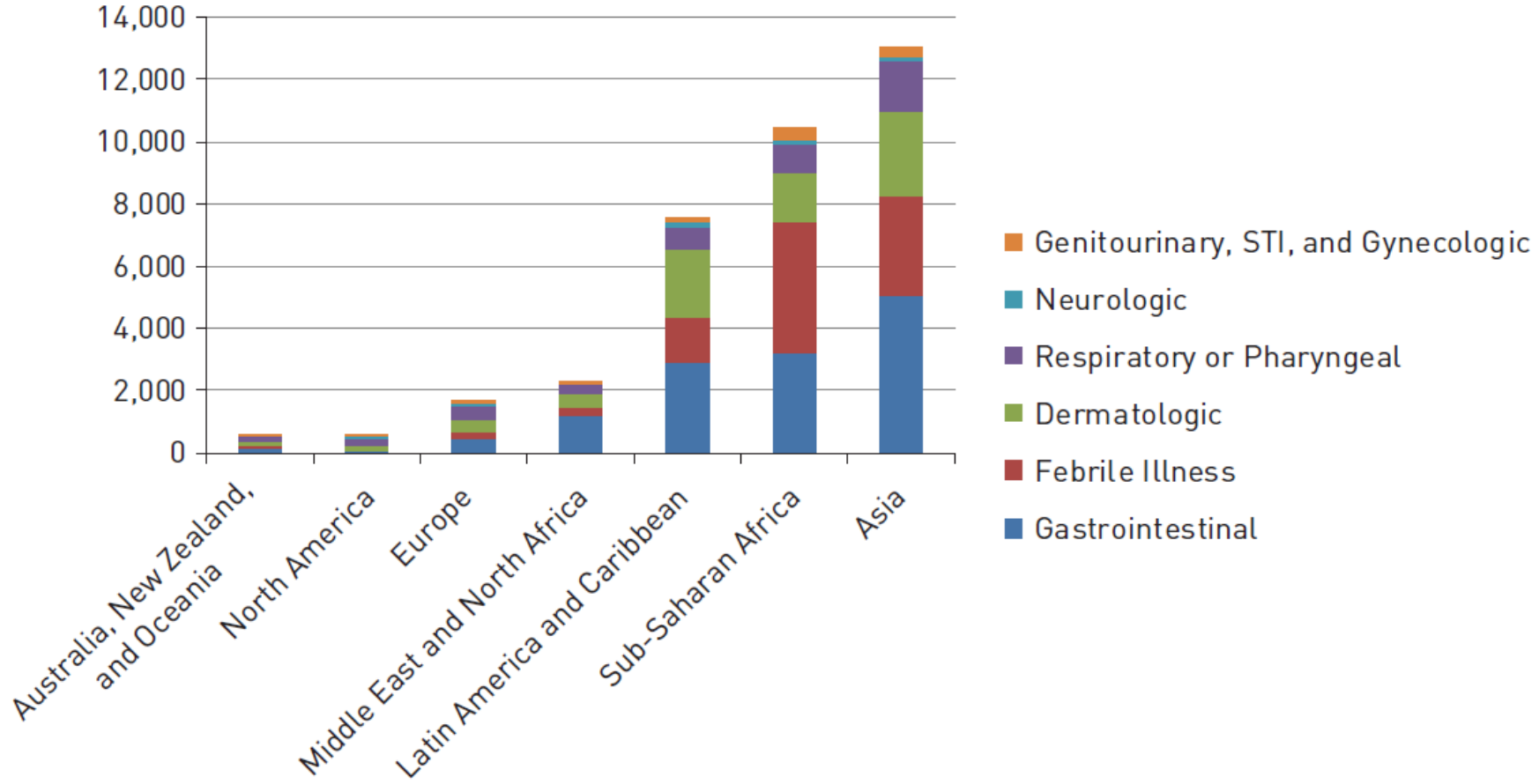
  (~ 4 million travelers)
- Most common illnesses: diarrhea, fever, and skin disorders

CDC Health Information for International Travel 2012. New York; Oxford University Press: 2012

Highest Risk for Travel-Related Illness

- Adventure travelers
- Persons who travel on a long-term basis
- Low-budget travelers
- Persons traveling back to country of origin
- Persons who are immunocompromised
- Age > than 65 years old

Illness in returned travelers, 2007–2011



Ann Intern Med. 2013 Mar 19;158(6):456–68.

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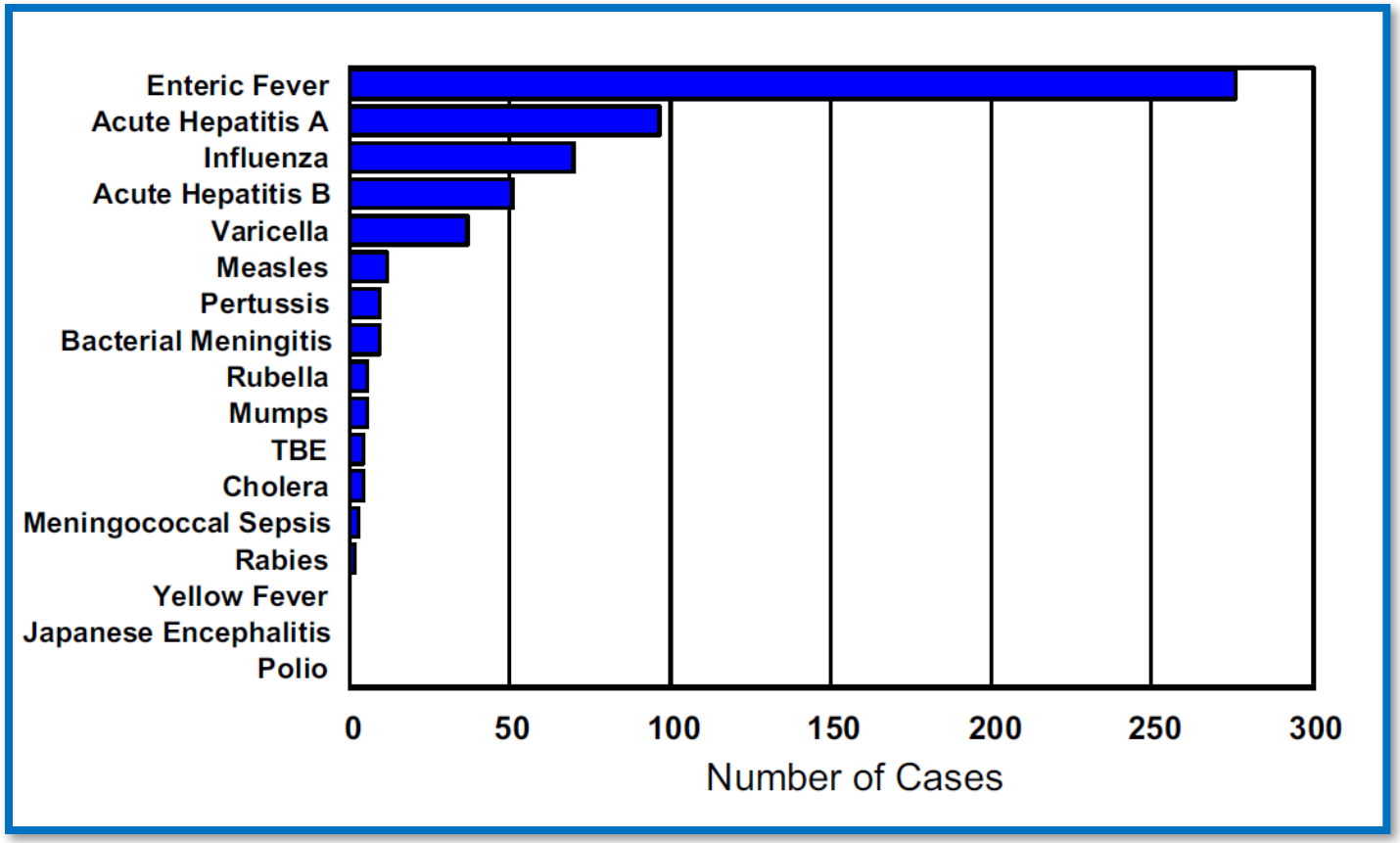
Vaccine Preventable Illness in Returning International Travelers



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Boggild AK, et al. Vaccine 28 (2010) 7389-7395

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Pre-Travel Consultation

- Countries, regions, flight layovers?
- Urban or rural?
- Possible activities – hiking, rafting, safari, camping?
- Accommodations?
- Who will be preparing your food?
- Are you visiting friends or relatives (VFRs)?

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General Advice for Travelers

- Carry letter stating medical dx and list of meds
- Carry enough essential meds to last longer than entire trip
- Jet lag
  - Avoid important activities on first day of travel
  - May give short course of sleep medication
- Motion sickness
- DVT prevention

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Food and Water

- Eat well-cooked hot foods
- Self-peel fresh fruits and vegetables
- Avoid:
  - Non-bottled beverages
  - Ice cubes
  - Unpasteurized dairy products
  - Food from street vendors
- Use bottled water to brush teeth

Vector borne disease prevention

- Insect repellants with 20 - 30% DEET
- Long sleeves, lighter colors clothing
- Bed netting
- Avoid perfumes, after shaves, etc.

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Case #1

- 30 y/o medical resident presents with fever of unknown origin.
- Traveled to India for medical mission work six weeks ago
- Intermittent fevers to 102 accompanied by malaise and fatigue.
- Labs: Hct 35, plt 140, normal LFTs
- Treated empirically for malaria 5 weeks ago with atovaquone/proguanil

What is the most likely diagnosis?

A. Typhoid fever (chronic carrier)
B. Mononucleosis
C. Dengue
D. Malaria

Plasmodium vivax

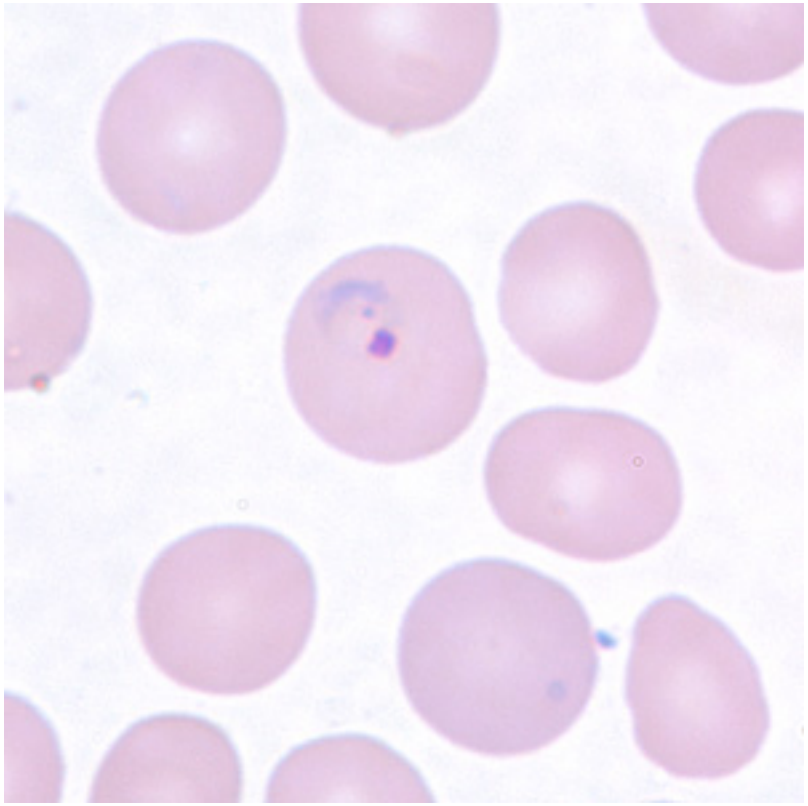


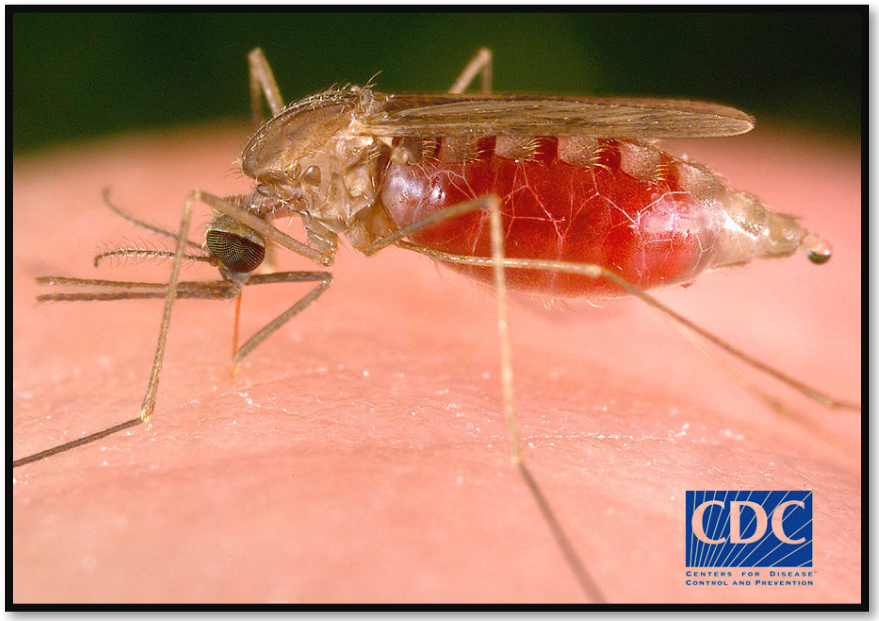
Image courtesy of cdc.gov

Plasmodium vivax

- Nine percent of all malaria cases
- Most dominant cause of malaria outside of Africa
- Life cycle includes hypnozoites – dormant stages in the liver that can reactivate weeks, months, years later
- Treatment of blood stage needs to be followed by primaquine to eliminate the liver stage

Malaria

- Genus *Plasmodium*
  - *P. falciparum*
  - *P. vivax*
  - *P. ovale*
  - *P. malariae*
  - *P. knowlesi*
    - Papua New Guinea
    - Malaysia



Female *Anopheles* mosquito

Image courtesy of cdc.gov

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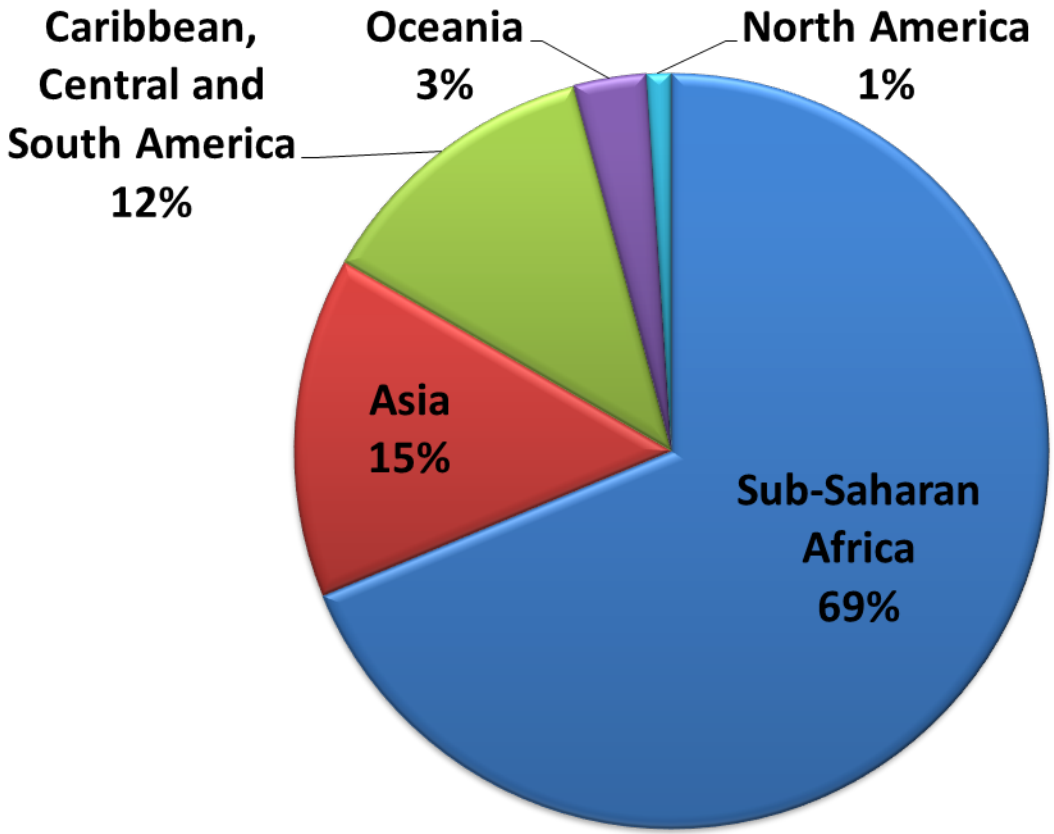
Malaria

- United States
  - 1,000-2,000 cases / year
  - 5-10 deaths / year
- Worldwide in 2015
  - 214 million clinical episodes
  - ~ 500,000 deaths
- Poor prognostic factors
  - Delay in diagnosis and therapy
  - Failure to treat complications (e.g. hypoglycemia)
  - Incorrect fluid/electrolyte management
  - Failure to monitor clearance (parasitemia)

Travel-Associated Malaria in US Residents



1999-2008
8,117 cases

CDC Health Information for International Travel 2012. New York; Oxford University Press: 2012

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Malaria Prophylaxis (non-pharmaceutical)

- *Anopheles* mosquitoes feed between dusk and dawn
- Mosquito bed nets
- Mosquito repellents
  - DEET (> 10%)
  - Picaridin
  - Oil of lemon eucalyptus
- Permethrin-treated clothing

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Malaria Chemoprophyaxis

- ALL must be taken before, during, and after trip
- No drug is 100% protective, must still be combined with personal protective measures
- Choosing a regimen
  - Itinerary
  - Drug-drug interactions
  - Potential side effects
  - Cost

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Image courtesy of cdc.gov

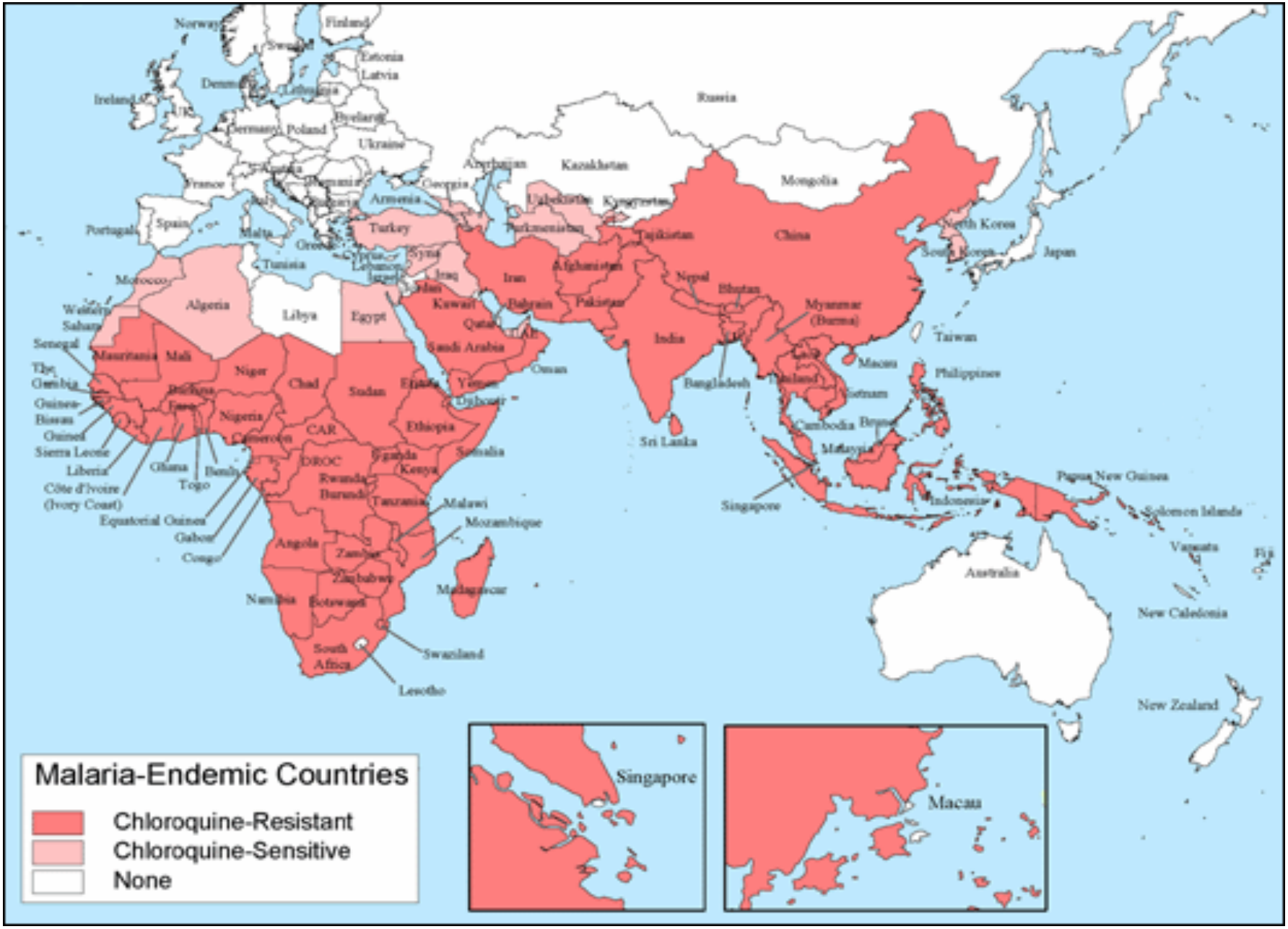


Image courtesy of cdc.gov

Atovaquone-proguanil (Malarone)

Countries	• All destinations
Dose	• 250 mg/100 mg, DAILY • 2 days before travel + daily + 7 days after leaving
Pediatrics/ Pregnancy	• Cannot be used in children < 5 kg • Cannot be used in pregnancy
Cost	• ~ $5/pill
Side Effects / Other	• Well tolerated • Contraindicated if CrCl < 30 mL/min

Doxycycline

Countries	• All destinations
Dose	• 100 mg DAILY • 2 days before travel + daily + 4 weeks post travel
Pediatrics/ Pregnancy	• Contraindicated in children < 8 years of age • Contraindicated in pregnancy
Cost	• ~$1/pill
Side Effects / Other	• Can also prevent rickettsial infections and leptospirosis • Vaginal yeast infections, increased sun sensitivity

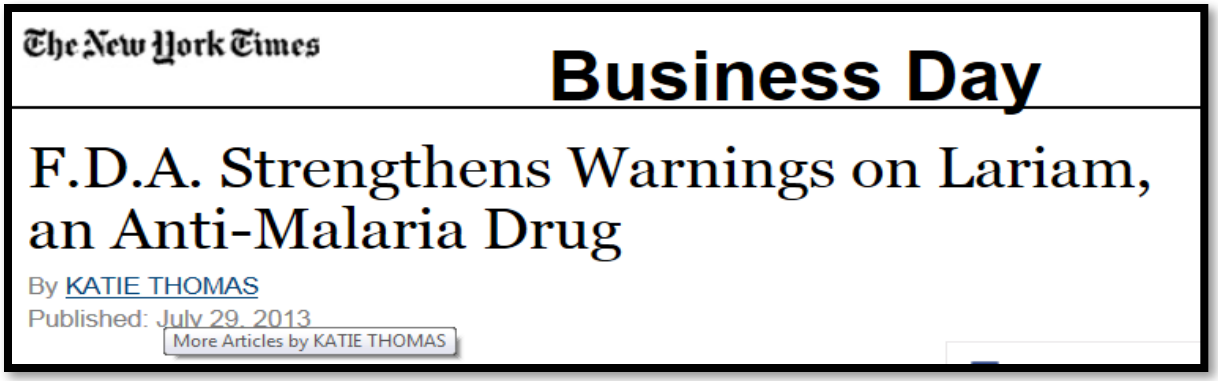
Chloroquine (Hydroxychloroquine)

Countries	• Limited • Central America, Haiti, Dominican Rep.
Dose	• 300 mg base (500 mg salt), WEEKLY • 2 wks before travel + weekly + 4 weeks post travel
Pediatrics/ Pregnancy	• Infants/children – weight based • All trimesters of pregnancy
Cost	• 150 mg base (#50): $123.00
Side Effects / Other	• May exacerbate psoriasis • Absorption may be reduced by antacids

Mefloquine

Countries	• Most destinations • Resistant areas – Burma, Laos, Thailand, Cambodia
Dose	• 228 mg base (250 mg salt), WEEKLY • 2 weeks before travel + weekly + 4 weeks after leaving
Pediatrics/ Pregnancy	• Infants/children – weight based • Can be used in 2nd and 3rd trimesters of pregnancy
Cost	• 250 mg (25) - $264
Side Effects / Other	• Contraindicated in pts with active depression, hx of depression, anxiety, seizures, cardiac conduction abnormalities……

Mefloquine



The New York Times

Business Day

F.D.A. Strengthens Warnings on Lariam, an Anti-Malaria Drug

By KATIE THOMAS

Published: July 29, 2013

More Articles by KATIE THOMAS

- Boxed Warning
  - Neurologic side effects
    - Can occur at any time, may be permanent
    - Dizziness, loss of balance, ringing in the ears
  - Psychiatric side effects
    - Feeling anxious, mistrustful, depressed
    - Hallucinations

www.fda.gov/Safety/MedWatch

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- Post-travel evaluation

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Pre-Travel Consultation

Routine Vaccines

DTaP
Hepatitis A, B
Hib
Herpes zoster
Influenza
MMR
Pneumococcal
Polio
Tetanus
Varicella

Travel-Related Vaccines

Hepatitis A/B
Typhoid fever
Yellow fever
Meningococcal
Polio (adult booster)
Rabies
Japanese encephalitis
Cholera

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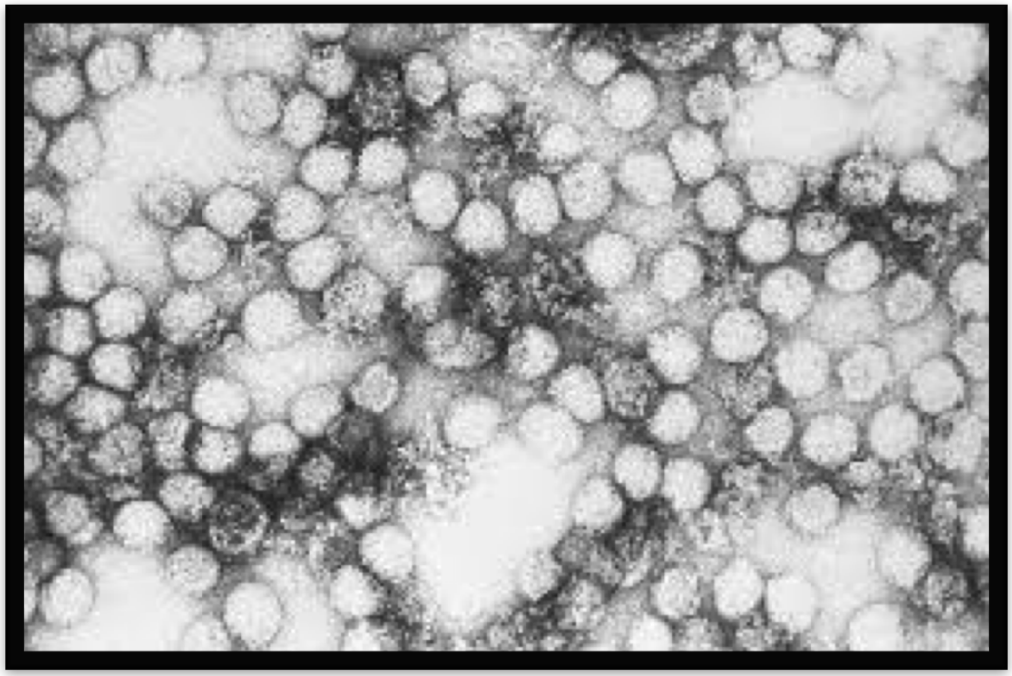
Yellow Fever



Electron micrograph of Yellow Fever Virus virions
CDC Public Health Image Library (PHIL)

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Yellow Fever

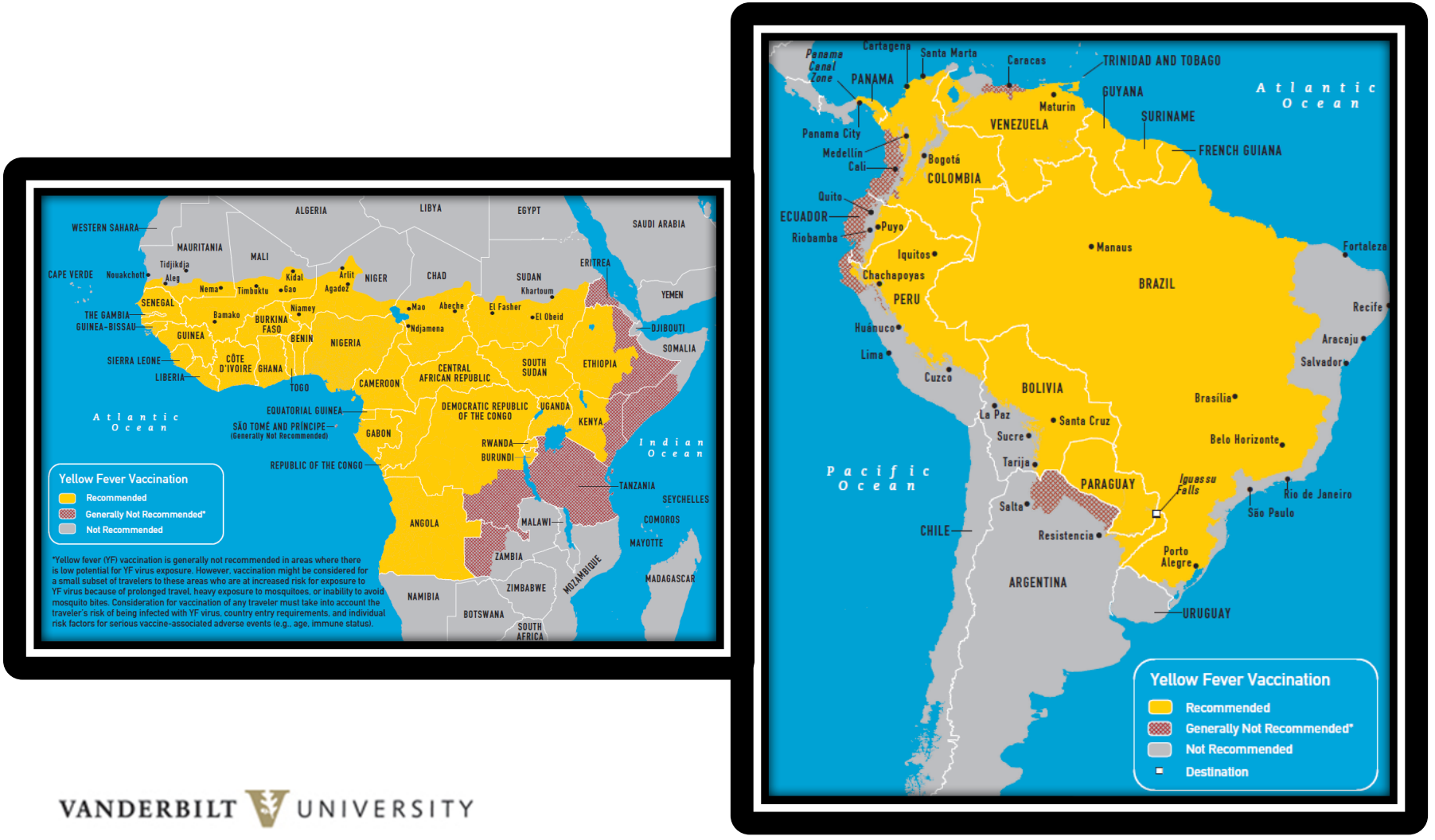

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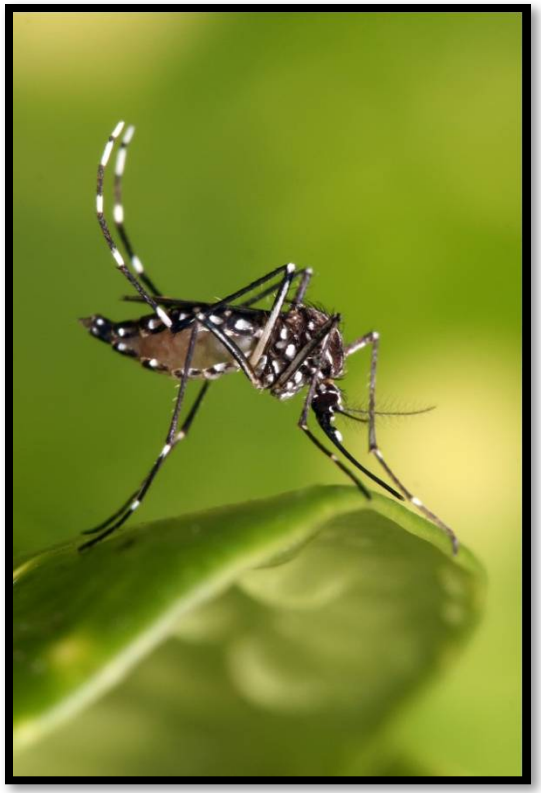
Image courtesy of cdc.gov

Yellow Fever

- *Flavivirus*
- Most are asymptomatic
- 3-6 day incubation period
- Nonspecific flu-like illness
  - Improvement
  - Short remission → jaundice, hemorrhagic shock, and organ failure (15% of pts)



Aedes aegypti

CDC Health Information for International Travel 2012. New York; Oxford University Press: 2012

Yellow Fever Vaccine

- Live attenuated
- May 2013
  - "WHO Strategic Advisory Group of Experts recently concluded that a single dose of yellow fever vaccine is sufficient to confer sustained immunity and lifelong protection against yellow fever disease"
  - Consider a booster if it's been 10 years and heading to a country with ongoing outbreak

Yellow fever vaccine - shortage

- Recent manufacturing issue has led to shortage of the only U.S.-licensed vaccine

- Sanofi Pasteur and FDA have collaborated to make an equivalent vaccine available to a small number of clinics (Stamaril)

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Yellow Fever Vaccine

Country entry requirements ≠ CDC recommendations

- Entry requirements are established by countries
- Must comply for entrance to country
- Person flying from US to South Africa, with a refuel in Senegal, MUST have proof of yellow fever vaccine, even if you remain on the plane.

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Yellow Fever Vaccine - Contraindications

- Age < 6 months (PRECAUTION age 6-8 months)
- Immunosuppressed – HIV/AIDS, transplant, medications
- Caution in persons >60y/o

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Yellow Fever Vaccine - Safety

- Mild systemic adverse reactions (10%-30%)
  - Headache, low-grade fever, myalgias – up to 10 days
- Hypersensitivity
    - Urticaria, rash, bronchospasm
    - Anaphylaxis (1.8 cases/100,000 doses)
- Yellow fever vaccine-associated neurologic disease (YEL-AND), rarely fatal
- Yellow fever vaccine-associated viscerotropic disease (YEL-AVD) – 65% fatality rate

CDC Health Information for International Travel 2012. New York; Oxford University Press: 2012

Typhoid and Paratyphoid Fever

- *Salmonella enterica* serotype Typhi
- Salmonella Paratyphi A, B or C
- Consumption of contaminated water/food
  - Acutely infected carrier
  - Convalescent carrier
  - Chronic, asymptomatic carrier

Image courtesy of Wikipedia

Typhoid and Paratyphoid Fever

- Risk is highest in Southern Asia
- Incubation period 6-30 days
- GRADUALLY increasing fatigue, fever/chills, abdominal pain
- Transient, rose-colored macular rash – trunk
- Can lead to intestinal perforation, death

http://doctorkd.blogspot.com

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Typhoid Vaccine

- Does **NOT** protect against *S. Paratyphi* infections

	ORAL (live)	INTRAMUSCULAR
Dose	One capsule Q48 hrs x 4	One dose
Lower age limit	6 y/o	2 y/o
Booster	Every 5 years	Every 2 years
Storage	Refrigerated	N/A
Contraindicated	Immunocompromised pts, Hx of Crohns, UC	N/A
Other	Avoid taking with antibiotics	Can be given with other vaccines (e.g. YFV)

Other Vaccinations

- Hepatitis A/B
- Rabies
- Japanese Encephalitis
- Meningococcal
- DTaP
- Cholera – refugee/
  aid workers

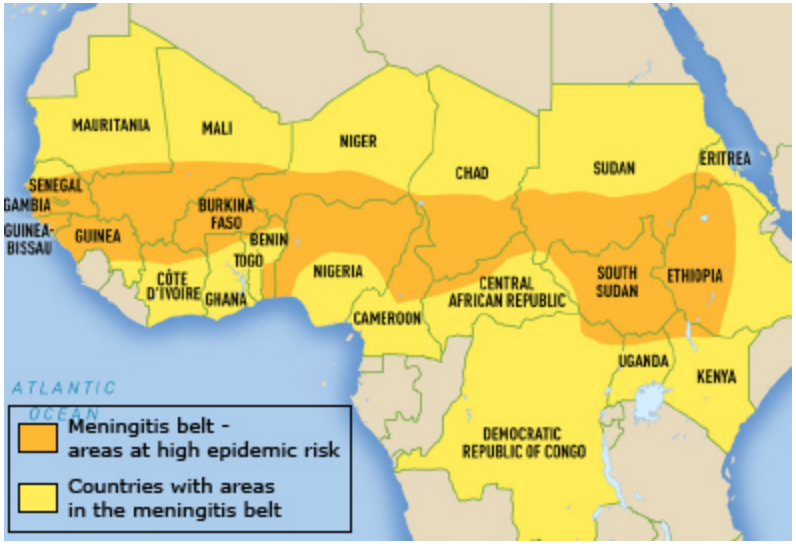

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Image courtesy of cdc.gov

Malaria

Lennart Nilsson, *Smithsonian* magazine, September 2012

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Outline

- Epidemiology
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  - **Self-treated and/or self-limited conditions**
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Travelers' Diarrhea

- High attack rate (up to 70%)
- Infection usually self-limited, dehydration may be severe
- Bacterial pathogens:
  - Enterotoxigenic *E. coli* (12%)
  - *Salmonella spp.* (8%)
  - *Campylobacter* (6%)
  - *Shigella spp.* (0.3%)
- Viral pathogens – norovirus, rotavirus
- Protozoa – *Giardia, Entamoeba, Cryptosporidium*

Adachi, et al. *CID*; 2001

Travelers' Diarrhea

- Symptoms:
  - Malaise, anorexia, abdominal cramps, sudden onset of watery diarrhea
  - Usually resolves 24-48 hours
  - Bloody stool/colitis – more suggestive of *Campylobacter* and *Shigella*
  - Belching, nausea – suggestive of *Giardia*
  - Post-infectious irritable bowel syndrome

Travelers' Diarrhea (TD)

- Treatment
  - Depends on severity – most cases just need fluid replacement
  - Loperamide (if no colitis)
  - Antibiotics – severe diarrhea, colitis, fever
    - Fluoroquinolones – Ciprofloxacin 500 mg BID x 3 days
      - Resistance in Southeast Asia (*Campylobacter)*
    - Azithromycin 500 mg daily x 3 day or 1g once
    - Rifaximin – 200mg PO TID x 3 days
      - *Campylobacter* are resistant, unclear utility in colitis

Case # 2

- 55y/o healthy female co-worker returns from a trip to Belize – “can you come look at this itchy rash?”

Photo courtesy of Dr. Julie Reznicek

Case #2

- Belize
- Resort area
  - Only resort food
- Day trips
  - Snorkeling
  - Scuba diving

- Symptoms
  - Rash began on back first, within 24 hours of water exposure
  - Abdominal rash developed one day later
  - NO systemic symptoms

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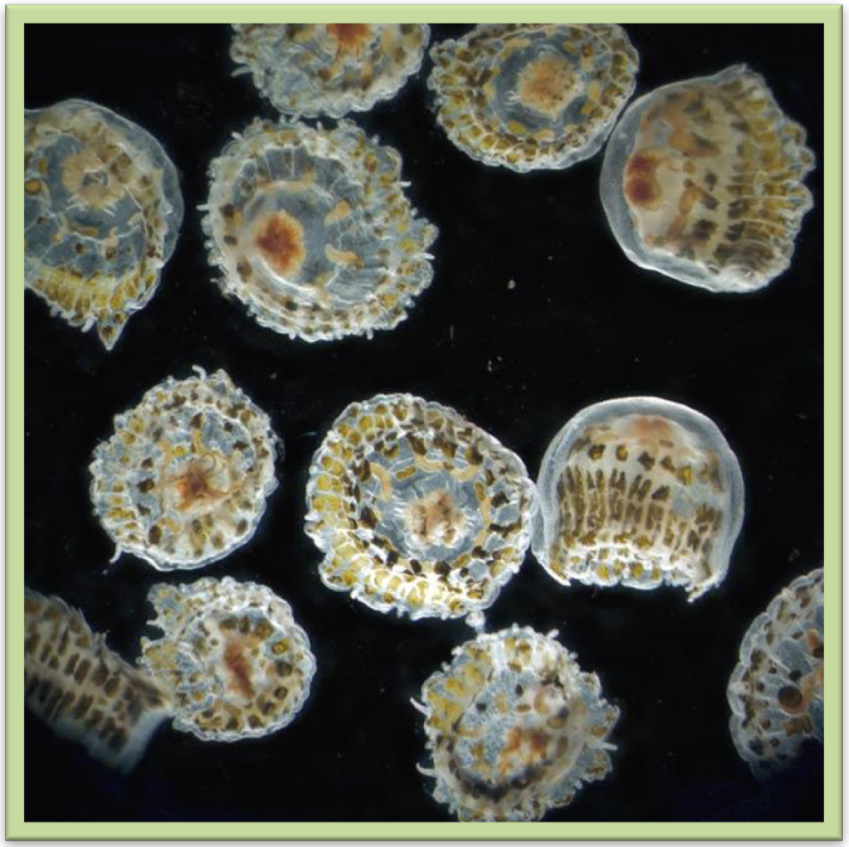
What is the most likely diagnosis?

A. Shingles
B. Drug Eruption
C. Parasitic infection
D. Jellyfish sting

Seabather's Eruption (Jellyfish Stings)

- Pruritic dermatitis
- Florida, Caribbean, Central America, Bahamas
- **Typically on skin covered by bathing suit**
- Jellyfish and sea anemone larvae become trapped
- Systemic symptoms (e.g. fever, malaise) very rare

Linuche unguiculata



www.cmarz.org

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Seabather's Eruption (Jellyfish Stings)

- Diagnosis
  - Distribution – areas covered by bathing suit, wet suit
  - Characteristics – inflammatory papules, vesicles
  - Skin scraping or sticky tape, looking for nematocysts
- Treatment
  - Nematocyst removal
    - Brushed off with plastic card
    - Hot water immersion
    - Topical steroids

Swimmer's itch

- Penetration of skin by nonhuman (usually avian) schistosomes
- Usually fresh water exposure
- Itchy, maculopapular rash (sometimes vesicular) **involving all areas exposed to water**

Medicinenet.com

Myiasis – Dermatobia hominis "botfly" or "mango fly"

- Insect bite that enlarges over time
- Patients may have sense of irritation or crawling
- Use occlusive dressing/petroleum jelly/bacon to suffocate for 24hrs, when dressing removed, grasp with tweezers as it comes up for air.

Case #3

A 22 y/o female medical student with “a spot on my foot.”

- Mozambique – returned one month ago
- Spent time on beach, walked barefoot
- Back in U.S. – spent time at an Ohio lake – first noted “spot” on left 4th toe.
- Identical lesion developed under toenail on adjacent toe.
- “Scab” fell off the 4th toe - presented to the ID clinic with this skin specimen in hand.

Case #3

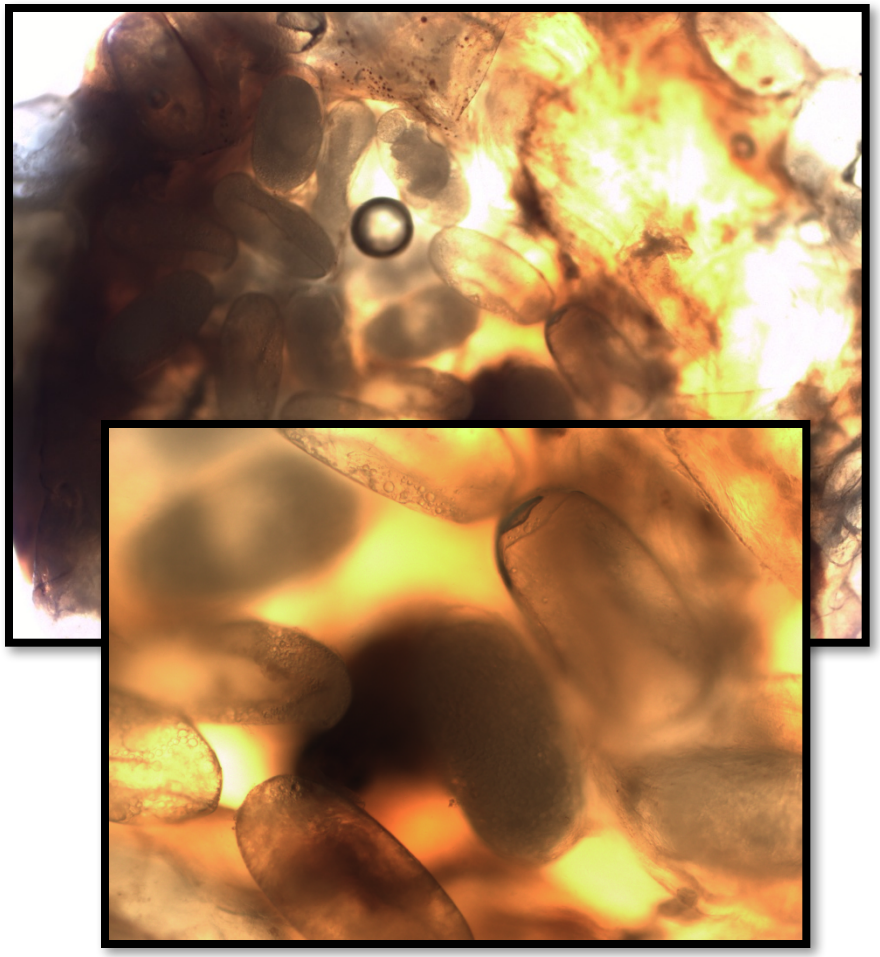

Photo courtesy of Dr. Julie Reznicek

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What is the most likely diagnosis?

A. Plantar wart
B. Foreign body
C. Insect bite
D. Parasitic infection

Tungiasis

- Sand flea (*Tunga penetrans*)
- Female burrows into skin
- Surgical extraction

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web.stanford.edu

Altitude Sickness

- Risks
  - Altitude - 8,000 ft (2,500 m)
  - Rate of ascent
- Clinical Presentation
  - Acute Mountain Sickness (AMS)
    - VERY common, “alcohol hangover”
  - High-Altitude Cerebral Edema (HACE)
    - AMS, lethargy, ataxis – MUST descend
  - High-Altitude Pulmonary Edema (HAPE)
    - Breathlessness at rest – MUST descend

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Altitude Sickness

- Treatment
  - Non-pharmacologic
    - Ascend gradually
    - Avoid alcohol
    - High-altitude exposure (> 9,000 ft) within 30 days of trip
  - Medications
    - Acetazolamide (contraindicated if allergic to sulfa)
    - Dexamethasone

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Evaluation of Returning Traveler

- Itinerary – including layovers
- Timing of exposure
- Timing of presentation
- Vaccines and prophylaxis
- Sexual history

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Evaluation of Returning Traveler

- Top causes of fever in returning traveler:
  - Malaria
  - Dengue
  - Typhoid fever
  - Mono (EBV or CMV…or acute HIV)
  - Rickettsial disease

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Case #5

- 11y/o boy with no significant past medical history presents to clinic with rash and fever
  - Returned from a trip to Haiti 5 days prior
  - Vomiting and diarrhea began 3 days prior
  - One day prior to admission – temp to 103°
  - Crying in pain from myalgia, headache, eye pain
  - Day of admission developed rash

- WBC 3.4, Hct 38, Platelets 199K, normal LFTs, creatinine 0.6

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What is the most likely diagnosis?

A. Malaria

B. Dengue

C. Typhoid fever

D. Zika infection

Case #1

- **Vector borne Diseases PCR Panel**

  Chikungunya PCR Results: Negative for Chikungunya virus by real-time RT- PCR
  Dengue PCR Results: Negative for Dengue virus by real-time RT- PCR
  Zika PCR Results: Positive for Zika virus by real-time RT- PCR

  Performing Location: Nashville

  Reference Range: Not Detected

  Disclaimer:
  Not FDA approved. Testing was performed under an emergency use authorization (EUA) from FDA. Information for the provider and the patient on the EUA can be obtained under, Zika Virus Emergency Use Authroization, Trioplex Real-time RT-PCR Assay (CDC) at http://www.fda.gov/MedicalDevices/Safety/EmergencySituations/ucm161496.htm#zika

  Comments:

  08/05/16 15:58 Virology **DENIgG**: 0.95 **DENIgM**: 1.41
  08/05/16 15:58 MiscHemes **MalSmr**: No malarial parasites present.

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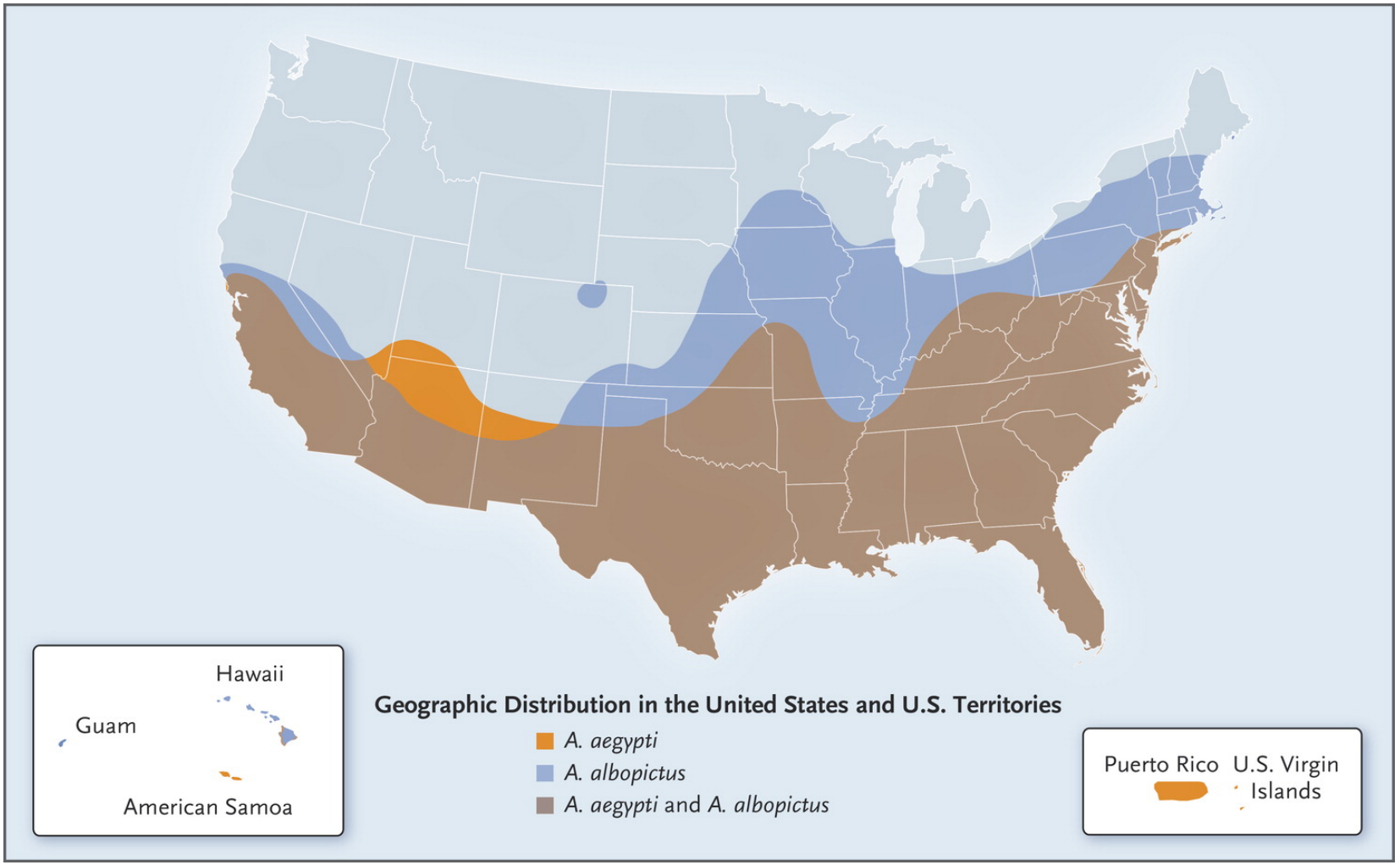
Zika Virus

- Flavivirus
- Single stranded RNA virus
- Main transmission
  - *Aedes aegypti*
  - *Aedes albopictus*
- Incubates 3-14d
- First isolated in Zika Forest of Uganda in 1947

Petersen LR et. al. NEJM 2016, CDC.gov

Approximate Ranges of *A. aegypti* and *A. albopictus* in the United States (as of March 2016).



Petersen LR et al. N Engl J Med 2016;374:1552-1563.

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Transmission

- Mosquito-borne
- Non-Mosquito borne
  - Maternal- fetal
    - Vertical transmission
    - Perinatal
  - Sexual transmission – vaginal, oral or anal
  - Likely through blood transfusion, transplant organs, breast feeding
  - Other animal bites
  - Laboratory exposure

Petersen LR et. al. NEJM 2016
CDC.gov

Zika Infection

- Infection rate: 73% (95% CI 68–77)
- Symptomatic attack rate among infected: 18% (95% CI 10–27)
- All age groups affected
- Adults more likely to present for medical care
- No severe disease, hospitalizations, or deaths
- Incubation period 3-14 days

Reported clinical symptoms among confirmed Zika cases, Yap Island, 2007

Symptoms	N (n=31)	%
Macular or papular rash	28	90%
Subjective fever	20	65%
Arthralgia	20	65%
Conjunctivitis	17	55%
Myalgia	15	48%
Headache	14	45%
Retro-orbital pain	12	39%
Edema	6	19%
Vomiting	3	10%

Duffy M et. al NEJM; 2009

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Differential diagnosis

- Dengue
- Chikungunya
- Leptospirosis
- Malaria
- Rickettsia
- Rubella
- Measles
- Parvovirus
- Enterovirus
- Adenovirus

Features	Zika	Dengue	Chikungunya
Fever	++	+++	+++
Rash	+++	+	++
Conjunctivitis	++	-	-
Arthralgia	++	+	+++
Myalgia	+	++	+
Headache	+	++	++
Hemorrhage	-	++	-
Shock	-	+	-

Rabe, Ingrid MBChB, MMed "Zika Virus- What Clinicians Need to Know?" (presentation, Clinician Outreach and Communication Activity (COCA) Call, Atlanta, GA, January 26 2016)

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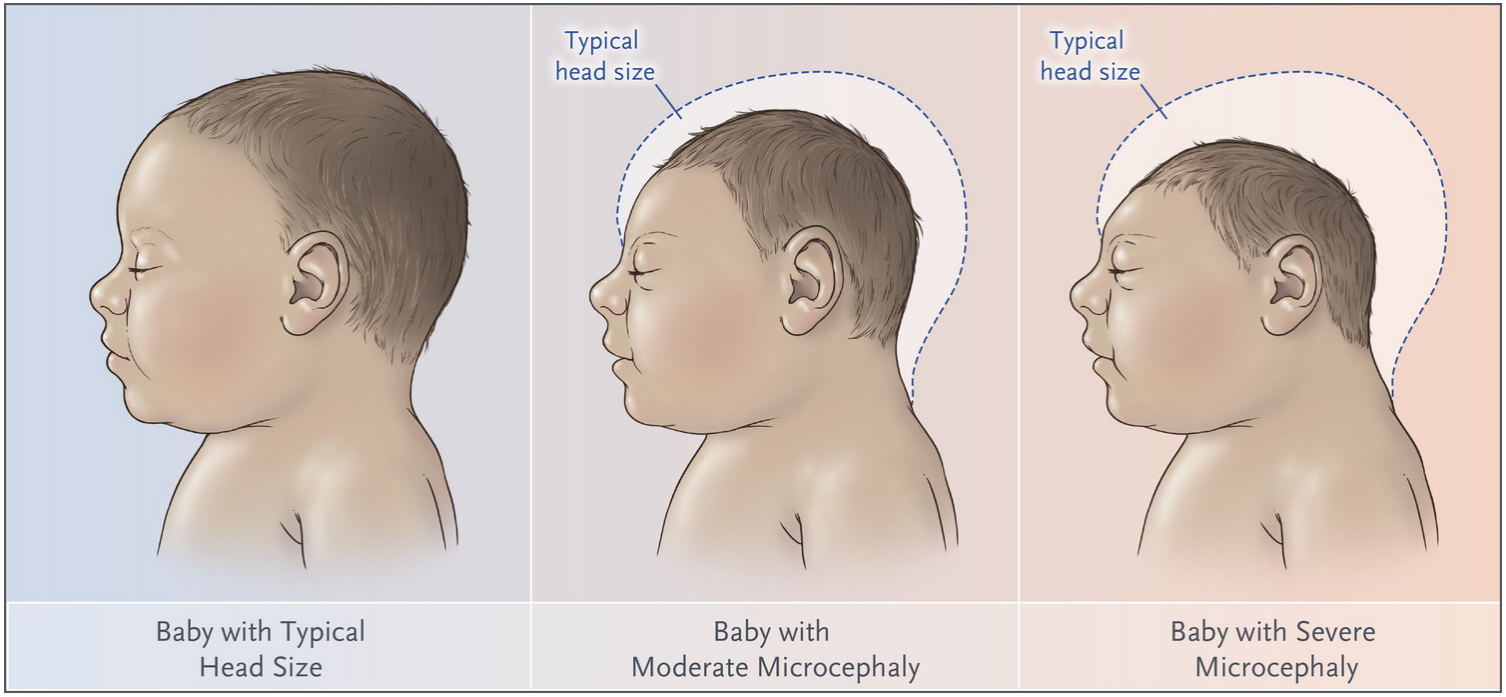
Neurologic complications

- Guillain-Barre
- Meningoencephalitis and myelitis



NEJM; Petersen, 2016
CDC.gov

Zika - Diagnosis

- RT-PCR and IgM antibodies (ELISA)
  - Viremia is low level and transient
  - RT-PCR most likely positive within 1 week after onset of clinical illness (longer in pregnant women whose fetus is infected)
  - RT-PCR may be detected longer in urine (14 days) than serum (7 days)
  - IgM may be positive in serum up to 12 weeks after illness onset

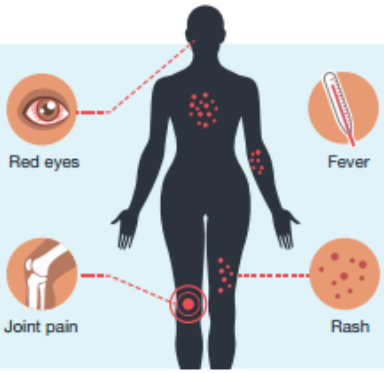
Who can be tested at the TDH?

- Symptomatic individuals within 2 weeks of travel to affected areas
- Any pregnant female who has travelled to affected area during pregnancy
- Any pregnant female if they had unprotected sex with a man confirmed to have Zika infection

CDC's Response to **Zika**

WHEN TO TEST FOR ZIKA VIRUS

As a healthcare provider, you decide if a patient should be tested for Zika virus infection. The algorithm below will help you determine whether or not to test your patient for Zika virus infection. For information on which test to use, see CDC's interim guidance.



If your patient is

- Experiencing or has recently experienced symptoms of Zika*
- An asymptomatic pregnant woman

Ask the following questions

Does the patient live in or has the patient recently traveled to an area with Zika?

- NO
- YES → **Test for Zika**

Has the patient had unprotected sex with a partner who has lived in or traveled to an area with Zika?

- NO → **Do Not Test for Zika**
- YES → **Test for Zika**

On blood products …

- 8/26/2016 – FDA recommended testing of donated whole blood and blood components
  - "At this time, the recommendation for testing the entire blood supply will help ensure that safe blood is available for all individuals who might need transfusion"

CDC.gov

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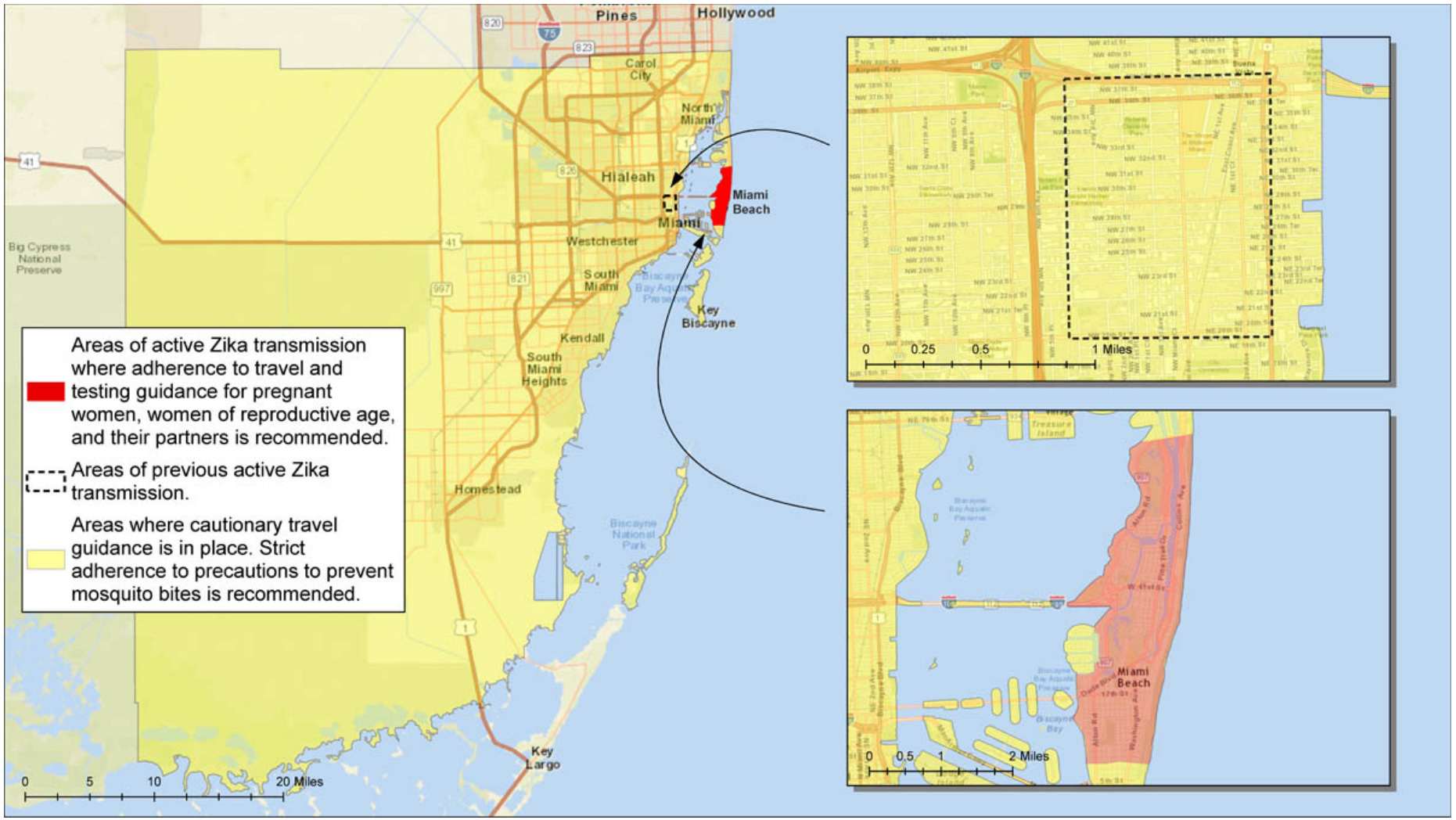
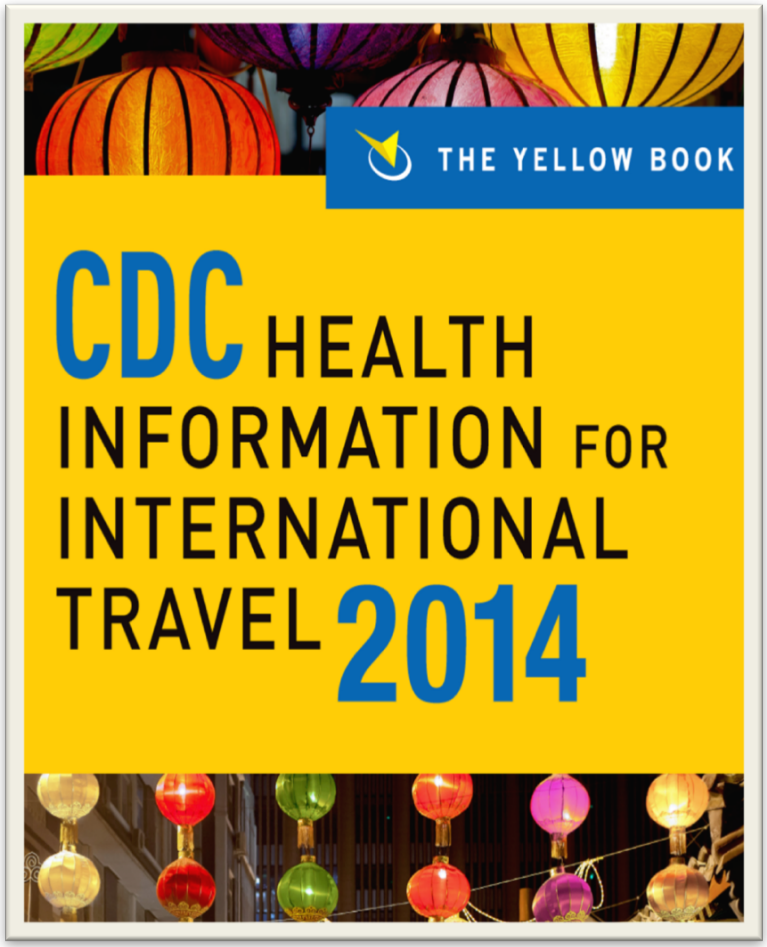

Areas of active Zika transmission where adherence to travel and testing guidance for pregnant women, women of reproductive age, and their partners is recommended.
Areas of previous active Zika transmission.
Areas where cautionary travel guidance is in place. Strict adherence to precautions to prevent mosquito bites is recommended.
Pines
Hollywood
Carol City
North Miami
Hialeah
Miami Beach
Miami
Westchester
South Miami
Kendall
South Miami Heights
Key Biscayne
Homestead
Biscayne National Park
Key Largo
Big Cypress National Preserve
0 5 10 20 Miles
0 0.25 0.5 1 Miles
0 0.5 1 2 Miles

Resources



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Resources

- www.cdc.gov/travel

- Geosentinel
  - Surveillance of travel-related morbidity

- www.travax.com
  - $895 per year
  - Destination / Route builder
  - Patient handout

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Questions?

Schedule Your Appointment Early

Immunizations require at least 14 days before travel to be effective.

Vanderbilt Travel Clinic

1301 Medical Center Drive, TVC Suite 2501, Nashville TN 37232

Phone: (615) 936-1174 - Fax: (615) 343-1691

Map and Directions

8 a.m.-5 p.m. Monday - 8 a.m.-1 p.m. Wednesday - 8-11 a.m. Friday