Travel in Pregnancy 2020: What to do when my pregnant patient plans to travel
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Travel During Pregnancy: Beyond Zika
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• No conflicts of interest to report.
• The opinions presented are those of the presenter and do not necessarily represent the official position of CDC.
Disclosures

1. Before Zika, I rarely asked my patients about travel.
2. During Zika, I only asked my patients about travel to Zika-affected areas.
3. Now, I try to remember to ask all my patients about travel during pregnancy to assess their risk of infectious diseases associated with travel.

International Travel is Increasing

Common Travel Destinations
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Travel During Pregnancy
- 5-59% of women travel internationally during pregnancy
- Trips to see family and friends
- "Babymoon" or other pre-baby vacation
- Work trips
- Majority of pregnant women do not seek pre-travel advice
- If pre-travel advice is sought, it's close to time of travel

Antony et al. WMJ. 2017 Dec;116(5):205-209

CDC Recommendations for Pregnant Travelers

Pre-travel Care and Travel Health Insurance
The first thing you should do when planning an international trip is to make an appointment with a healthcare provider who specializes in travel medicine. You should ideally not be traveling at least 6 weeks before your due date. If you are traveling close to the end of your pregnancy, you may need to discuss with your doctor whether it is safe for you to travel. Your travel medicine doctor or your obstetrician should also be able to talk to each other about your care.


What about travel health insurance? Medical evacuation?


Pregnant Travelers

Pregnant women can generally travel safely with a little preparation. But they should avoid some destinations, including those with Zika and malaria risk. Learn about when you can take if you’re pregnant and planning an international trip, especially to a developing country. Follow these tips to keep you and your baby safe and healthy.


Resources
- Zika and Malaria
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Zika Travel Recommendations

- CDC Zika travel guidance: January 2020
  - Pregnant women should not travel to areas with Zika outbreaks, and should talk to their HCP about risks and possible consequences before traveling to an area with current or past transmission of Zika.

- WHO travel guidance: January 2020
  - Pregnant women avoid travel to areas with Zika virus transmission, particularly during outbreaks, based on the increased risk of microcephaly and severe congenital malformations in infants born to women infected with Zika virus during pregnancy.
  - If pregnant women or women who may become pregnant must travel, talk with HCP and consider risks and possible consequences of infection before traveling to areas where there may be Zika virus transmission.

CDC Zika Clinical Guidance: A History

- 2016: Initial travel & pregnancy guidance
- 2017: Updated travel & pregnancy guidance
- 2018: Updated pregnancy guidance
- 2019: Updated guidance for women of reproductive age

Map Legend:
- Current or recent Zika outbreaks
- Countries that have ever reported Zika
- Countries with travel restrictions
- Countries with Zika cases
- Countries with no reported Zika

World Map of Areas with Risk of Zika


Updated testing guidance: June 2016
Updated pregnancy guidance: Jan 2016
Initial travel & pregnancy guidance: Feb 2016
WHO declarations initial Feb 2016

Jan: Initial travel & pregnancy guidance
Feb: Updated travel guidance
July: Updated pregnancy guidance
Aug: Updated guidance for women of reproductive age
Oct: Updated guidance for women and men of reproductive age
Feb: WHO declares PHEIC
Nov: WHO declares end of PHEIC
Apr: First guidance for women of reproductive age
June: Updated testing guidance
Aedes aegypti mosquitoes also transmit dengue virus
Honduras experiencing outbreak of dengue, 34k cases, ~60 deaths
Currently (Jan 2020) dengue infections outnumber Zika 200:1

CDC Updated Testing Recommendations: June 2019
Symptomatic pregnant women should receive Zika and dengue virus testing concurrently
Testing recommendations for asymptomatic pregnant women have not changed

Dengue During Pregnancy
- Perinatal transmission can occur
- Increased risk of adverse outcomes
  - Preterm birth (OR=2.4; 95% CI 1.3 to 4.4)
  - Low birthweight (OR=2.1; 95% CI 1.1 to 4.4)
  - Neonatal death (p<0.05 increase risk)
- Dengue infection in neonates can cause:
  - Thrombocytopenia
  - Ascites or pleural effusions
  - Fever
  - Hemorrhage
  - Hypotension
- Treatment: supportive
Pre-Travel Preparations

Pre-Travel Considerations
- Location specific risks for endemic diseases + outbreaks based on epidemiology*
- Existing immunity and immunization status
- Prophylactic medications
- Preventative behavior for insect, food, and water risks
- Emergency care options at destination

*Infectious disease surveillance varies widely by country

Pre-Travel Counseling: Patient A

26-year-old healthy woman at 20 weeks gestation comes for a OB visit & “surprise” pre-travel consultation. She will be going to Israel to visit family for 3 weeks.
- What are you concerned about?
- What guidance would you give her?
- Where would you get more information?
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Tools for Travel Recommendations

1. Pre-travel PREP
2. CDC's Travelers' Health Website
3. Heading Home Safely — info on post return to stay healthy (Mass Gen + CDC + TravEpiNet)

Recommendations for Patient A

- Routine vaccines
  - Tdap
  - Influenza
- Location-specific vaccines
  - Hepatitis A
  - Inactivated typhoid
- Preventative behavior
  - Avoid insect bites that may carry vector-borne diseases
  - Safe eating and drinking to avoid infectious diseases (e.g., Hep A, Listeria)
  - Wearing helmet/seatbelt

Additional Behavioral Precautions

- Good hand hygiene
- Contaminated food and water:
  - Traveler's diarrhea
  - Hep A and typhoid
- Parasitic infections
- Avoid tap water, ice made from tap water, raw foods rinsed with tap water
- Chlorination kills most bacterial and viral pathogens
- Protozoal cysts of Giardia, Entamoeba & oocysts of Cryptosporidium survive
- Boiled or treated water can be used
- Carbonated beverages, beer, wine and drinks made with treated water are safe
- Produce peeled by the traveler may be eaten (e.g., orange, banana)
- Food should be well cooked and eaten while hot
- Avoid unpasteurized dairy products and undercooked meat and fish
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Behavioral Precautions
- Avoid vector-borne diseases (malaria, dengue, chikungunya, Zika)
  - Wear clothing that reduces the amount of exposed skin
  - Use insect repellent
  - Insecticide treated fabrics
- Swimming & beaches
  - Avoid swimming in fresh water where schistosomiasis is prevalent
  - Swimming in chlorinated or salt water is safe
  - Rafting or exposure to flood waters can expose to leptospirosis
  - Walking barefoot or with open shoes on beaches, soil or water that may be contaminated with human or canine feces may lead to contact with hookworm or Strongoloides larvae
- Sunglasses and sunblock
- Avoid approaching animals
- Risks of animal bites and scratches, including rabies

Hepatitis A
- Pregnant women are not at an increased risk of hepatitis A infection nor do they experience more severe infection
- Maternal infection during pregnancy rarely results in adverse outcomes; some reports of preterm labor, placental abruption, premature rupture of membranes
- Pregnant women with travel-related risk should receive at least one dose of Hep A vaccine prior to travel: pregnant women appear less likely to get vaccine (28% vs 51%)
  - Inactivated vaccine so safe for pregnant women
- IgG is effective for post-exposure prophylaxis and can be administered during pregnancy if indicated

Typhoid Fever
- Fever may last longer among pregnant women
- Reports of intrauterine transmission, preterm birth and pregnancy loss
- Pregnant women with travel-related specific risk should consider the inactivated vaccine; oral vaccine is live attenuated so not preferred
  - Pregnant women less likely to get typhoid vaccination (28% vs 51%)
- Treatment
  - Antimicrobial therapy shortens the duration of fever and reduces the risk for death; however, antimicrobial resistance is widespread
  - Azithromycin is the drug of choice to treat multidrug-resistant strains causing uncomplicated disease; severe infections should be treated with a carbapenem
Pre-Travel Counseling: Patient B

31-year-old healthy woman at 30 weeks gestation comes for a pre-travel consultation.
She is planning to travel to Ghana for 1 week to attend a funeral of a family member.

- What are you concerned about?
- What guidance would you give her?

Recommendations for Patient B

- Consider postponing travel
- If traveling:
  - Routine vaccines
  - Location specific vaccines
    - Hepatitis A and B
    - Typhoid
  - Antimalarials
  - Preventative behavior
    - Avoid insect bites
    - Safe eating and drinking

Safe Eating & Drinking

- Good hand hygiene—also carry hand sanitizer
- Contaminated food and water:
  - Traveler’s diarrhea
  - Hepatitis A and E, Listeria
  - Parasitic infections such as toxo & schistosomiasis
  - Avoid tap water, ice made from tap water, raw foods, water
    - Chlorination kills most bacterial and viral pathogens
    - Parasitic cysts of Giardia, Entamoeba & oocysts of Cryptosporidium survive
  - Boiled or treated water can be used
  - Sealed carbonated beverages, beer, wine and drinks made with boiled water safe
  - Produce peeled by the traveler may be eaten (e.g., orange, banana)
  - Food should be well cooked and eaten while hot
  - Avoid unpasteurized dairy products and undercooked meat and fish

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2860824/
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Behavioral Precautions-2

- Avoid areas with VECTOR BORNE DISEASES (malaria, dengue, chikungunya, Zika)
- Wear long-sleeved shirts and pants and permethrin-treated clothing
- Stay in places with air conditioning or with door and window screens
- Sleep under an insecticide-treated bed net

Prevention of Mosquito-borne Diseases

- Use Environmental Protection Agency (EPA)-registered insect repellent*
  - DEET, picaridin, IR3535, oil of lemon eucalyptus, para-menthane-diol, or 2-undecanone
- Wear long-sleeved shirts and pants and permethrin-treated clothing
- Stay in places with air conditioning or with door and window screens
- Sleep under an insecticide-treated bed net

Malaria

- Pregnant women are at higher risk of severe disease and adverse pregnancy outcomes
- No prophylactic regimen provides complete protection
- Pregnant women should ideally avoid travel to malaria endemic areas. If travel is unavoidable, pregnant women should take precautions to avoid mosquito bites and use an effective prophylactic regimen

Recommended drugs
- Chloroquine
- Mefloquine (for areas with chloroquine-resistance)

Contraindicated drugs
- Doxycycline
- Primaquine (infant can’t be tested for G6PD deficiency)

https://www.cdc.gov/malaria/travelers/drugs.html
**Most Common Illness: Travelers’ Diarrhea**

- Attack rates of 30–70%
  - “boil it, cook it, peel it, or forget it” prevents most
- Enterotoxigenic E. coli is the most common cause, but other bacteria, viruses, and protozoa can cause illness
- Prevention measures include safe eating and drinking and proper handwashing, but prophylactic antibiotics may be considered for short-term travelers
  - Risks of prophylactic antibiotics weighed against benefit of prompt self-treatment when moderate/severe TD occurs, shortening duration of illness to 6–24 hours
  - Bismuth subsalicylate not recommended for pregnant women—otherwise can decrease TD by 50%

**Treatment of Travelers’ Diarrhea**

- For mild illness, oral rehydration therapy (ORT) is recommended
- For moderate illness, antibiotics may be used in addition to ORT
  - Azithromycin is the preferred treatment
- For severe illness, antibiotics should be used in addition to ORT
  - Azithromycin is the preferred treatment
- Pregnant women should seek medical care for any moderate to severe diarrhea because of risks of dehydration
- Severity is classified by illness’ functional impact
  - **Mild (acute):** diarrhea is tolerable, not distressing, and does not interfere with planned activities
  - **Moderate (acute):** diarrhea is distressing or interferes with planned activities
  - **Severe (acute):** diarrhea is incapacitating or completely prevents planned activities; all dysentery is considered severe

**Summary of Pre-Travel Considerations**

- Review
  - Location specific risks for endemic diseases + outbreaks based on epidemiology
  - Existing immunity and immunizations status
  - Prophylactic medications
  - Preventive behavior for insect, food, and water risks
  - Emergency care options at destination
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Post-Travel Considerations

Illnesses associated with fever within first 2 weeks post-travel

- Malaria
- Dengue
- Typhoid fever
- Rickettsial diseases (such as scrub typhus, spotted fever)
- East African trypanosomiasis
- Acute HIV infection
- Leptospirosis
- Flavivirus disease
- Viral hemorrhagic fevers

- Meningococcal meningitis
- Meningitis
- Arboviral encephalitis (such as Japanese encephalitis, West Nile virus)
- East African trypanosomiasis
- Hepatitis

- Influenza
- Bacterial pneumonia
- Acute histoplasmosis or coccidioidomycosis
- Legionella pneumonia
- Q fever
- Malaria
- Typhus
- Parvovirus B19
- Acute HIV infection
- Dengue
- Chikungunya
- Zika
- Malaria
- Parvovirus B19
- Acute HIV infection

Post-travel: Clinical Case #1

21-year-old healthy woman presents to your office at 22 weeks gestation with history of fever, malaise, cough, and conjunctivitis for 5 days and then developed a maculopapular rash. She has recently traveled to Ukraine to see her family.

What are you concerned about?
Post-travel: Clinical Case #1

On further questioning, she reports that several others in her family have had the same symptoms.

She then discloses that she has not been vaccinated for any infectious diseases because it is against her beliefs.

Clinical Presentation

Reported Measles Cases
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Recent Measles Cases in the US States

Measles and Pregnancy

- Pregnant women at higher risk for adverse outcomes
  - More likely to be hospitalized (60-96%)
  - More likely to develop pneumonia (10-40%)
  - More likely to die (3-18%)

- Increased risk of adverse pregnancy outcomes
  - Low birthweight (11-17%), preterm birth, admission to NICU
  - Possible association with spontaneous abortion, intrauterine fetal death, neonatal mortality
  - No conclusive evidence for birth defects

- Congenital measles (0-12.5%)
  - Mortality and panencephalitis

Treatment of Measles

- Measles incubation period ranges from 7 to 21 days from exposure to onset of fever; rash usually appears about 14 days after exposure

- Airborne isolation for 4 days after appearance of rash

- Supportive care

- Intravenous immunoglobulin within 6 days of exposure as post-exposure prophylaxis
24-year-old healthy woman presents to your office at 25 weeks gestation with high fever and flu-like symptoms 10 days after a 2-week trip to Nigeria. She reports staying in “rustic” accommodations, and sleeping with windows open.

- What are you concerned about?
- How does travel history affect your differential diagnosis?
- What could help you narrow the diagnosis?
Malaria During Pregnancy

- Uncomplicated malaria: symptoms present without signs of vital organ dysfunction
  - High fever, chills, sweats and headache
- Severe malaria: infection complicated by serious organ failures, abnormalities in the patient’s blood or metabolism, for example:
  - Neurologic, renal, respiratory or cardiovascular failure
  - Anemia, hypoglycemia, metabolic acidosis
  - Hyperparasitemia
- Congenital malaria is rare and resembles neonatal sepsis

Malaria Treatment

- Treatment depends on the *Plasmodium* species, drug resistance, and severity of disease
- CDC website lists drug resistance by country to inform treatment decisions
- **Uncomplicated malaria**
  - Chloroquine (if sensitive)
  - Quinine and clindamycin
  - Mefloquine
  - Artemether/Lumefantrine in 2nd and 3rd trimester (1st trimester too if no other options)
- **Severe malaria**
  - IV artesunate for 48 hours
  - After the course of IV artesunate is completed, a follow-up drug must be administered

Summary of Post-Travel Considerations

- Assess for symptoms; onset of illness relative to travel
- Determine
  - travel history (itinerary and duration)
  - exposure by country
  - behavior risks (insect precautions, food and water consumption, sexual activity)
  - Immunizations prophylaxis
- Prompt treatment
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Take Home

- Pregnant women are traveling more frequently; assess risk during prenatal care and monitor epidemiology
- Pre-travel planning and counseling can help pregnant women make informed travel decisions and prevent infectious diseases
  - Vaccines
  - Prophylaxis
  - Behaviors
- Post-travel awareness of exposure, symptoms and treatment options can mitigate adverse outcomes

Resources

- CDC Yellow Book
- CDC Travelers' Health Website
  - https://wwwnc.cdc.gov/travel
- Global TravEpiNet Pre-travel Prep Tool
  - https://gten.travel/prep/prep
- Malaria Information and Prophylaxis, by Country
  - https://www.cdc.gov/malaria/travelers/country_table
- Yellow Fever Vaccination Clinics

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The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.
**Human to Human Transmission**

Ebola virus can be found in all body fluids:

- Blood
- Feces/Vomit
- Urine
- Tears
- Saliva
- Breast milk
- Amniotic fluid
- Vaginal Secretions
- Sweat
- Semen

Contact (through a break in skin, mouth, eyes) with the body fluids of a person that is sick or has died of EVD.

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**Ebola Outbreak**

August 1, 2018 DRC declaration of outbreak

June 12 Spread to Uganda (3 cases)

July 17: WHO declared Public Health Emergency of International Concern

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**Outbreak Progression**

As of August 6, 2019:

- 2,781 total cases (2687 confirmed, 94 probable)
- 1886 total deaths (67% case fatality proportion)
- ~ 120 total healthcare worker infections
Ebola and Pregnancy

- Limited information
- No evidence of increased susceptibility
- Increased risk for severe disease and death
  - Maternal mortality about 90% in prior outbreaks, lower in 2014-2016 outbreak
- Increased risk for spontaneous abortion, stillbirth, and pregnancy-related hemorrhage
- High perinatal mortality rates among infants of Ebola-infected women
- Ebola virus can cross the placenta and maternal-fetal transmission is likely

https://www.cdc.gov/vhf/ebola/clinicians/evd/pregnant-women.html

Recombinant Vesicular Stomatitis Virus-Based Ebola Virus Vaccine

- Live vaccine containing a piece of Ebola virus
- Experimental
- Given as a single dose
- Protects only against Ebola virus (species Zaire ebolavirus)

Offered to:
- Contacts and contacts of contacts of EVD cases (deceased or alive) through a ring vaccination strategy
- Frontline healthcare workers

Eligibility criteria:
- Children >6 months of age
- Adults, including pregnant and lactating women

Treatment

- No FDA approved treatments for EVD
- Early supportive care alone can significantly improve chances of survival
- 4 experimental treatments approved for use in DRC through a randomized clinical control trial

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<thead>
<tr>
<th>Name of Drug</th>
<th>Type of Drug</th>
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<tr>
<td>ZMapp</td>
<td>Triple monoclonal antibody cocktail</td>
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<tr>
<td>Regeneron</td>
<td>Triple monoclonal antibody cocktail</td>
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<tr>
<td>mAb 114</td>
<td>Monoclonal antibody</td>
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<tr>
<td>Remdesivir</td>
<td>Antiviral</td>
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**Treatment**

- Pregnant women with EVD should be treated the same as any other adult
  - Provide fluids and electrolytes
  - Use oxygen therapy to maintain oxygen saturation
  - Support blood pressure
  - Reduce vomiting and diarrhea
  - Manage fever and pain
  - Treat other infections

- Obstetric management should consider risks to woman and potential benefits to neonate

**Management of Ebola and Pregnancy**

- History of travel within 21 days from DRC, or recent contact (within 21 days) with a person with Ebola virus disease (EVD), screen for fever and symptoms of EVD
  - If signs or symptoms of EVD, immediate isolation and appropriate infection control
  - Asymptomatic pregnant women who have no other epidemiologic risk factors should receive routine obstetric care
    - Risk factors include contact with: body fluids from a person with EVD, objects contaminated with body fluids, infected bats or primates, semen from a man with EVD

**Current Ebola Response Challenges**

- Complex humanitarian emergency
- >1 million internally displaced persons in DRC
- Continuous movement of refugees to neighboring countries, including Uganda, Rwanda, and South Sudan
- Incidents of violence against response teams & pockets of community resistance
- High number of EVD deaths occurring outside of an Ebola treatment unit in the community
- Low number of confirmed cases under surveillance as contacts at the time of notification
- Transmission chains linked to nosocomial exposures
- Delays in detection and isolation of cases
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**Response Efforts**
- DRC Ministry of Health leading response efforts, with assistance from local and international partners, including the World Health Organization (WHO)
- Response activities divided into pillars to include:
  - Surveillance
  - Infection Prevention & Control
  - Points of Entry
  - Safe and dignified burials
  - Laboratory
  - Logistics
  - Psychosocial
  - Case management
  - Community engagement
  - Security

**CDC’s role**
- United States government, including CDC, working with DRC MOH and other partners to provide technical assistance and expertise in several critical areas, including:
  - Surveillance
  - Data analysis/management
  - Emergency management
  - Infection prevention and control
  - Health communications
  - Vaccination

As of June 11, 187 CDC staff have completed 278 deployments to the DRC, Uganda, South Sudan, Geneva

**Figure** shows provisional data for laboratory-confirmed symptomatic Zika virus disease cases with illness onset in 2016–2018, reported to ArboNET by US states (excluding territories).

*Includes reported confirmed and probable Zika virus disease cases per the CSTE case definitions"