Mitigating the Impact of Mosquito-Borne Diseases on Children and Their Families

Susan E Coffin, MD, MPH
Children’s Hospital of Philadelphia
UPENN School of Medicine
March, 2017

Disclosures

• I have received support for participation in this conference from The Research and Regulatory Management Council, Washington, D.C.

• I have received research support from the NIH, CDC, AHRQ and the Thrasher Foundation.

Learning Objectives

• Identify the major mosquito-borne illnesses afflicting children in the U.S. and its territories.

• Discuss the transmission and clinical features of Zika virus infection.

• Present evolving recommendations about Zika for primary care clinicians.

• Discuss Zika treatment and prevention strategies.

Mosquito-borne Infections

• Worldwide “vector-borne” infections account for 17% of all infectious diseases
  — Responsible for > 1 million deaths/yr

• Mosquitoes most common and widespread
  — Over 3,500 species
  — Ubiquitous except…
    - Iceland
    - New Caledonia
    - The Seychelles
    - Antarctica

The Threat of Mosquito-borne Disease Isn’t New...

Current Mosquito-borne Diseases in the U.S.

• West Nile virus
• St. Louis Encephalitis
• Western Equine Encephalitis
• Eastern Equine Encephalitis
• LaCrosse Encephalitis

• Dengue
• Chikungunya
• Malaria*

Zika!
Disease Transmission

• Females of many species are “ectoparasites”
  – Require blood meal to produce eggs
• Preferred host varies by mosquito species
  – Mammals > birds > amphibians/reptiles > fish
• Inject saliva (anticoagulant properties) prior to sucking blood
• Host response to foreign proteins with histamine → wheal or “bite” with itchiness

Are You a Preferred Provider?

• Sensory organs on antennae
  – CO₂, octenol (sweat), sulcatone (human blood)
• Type O blood
• “Heavy breathers”
• Dense skin colonization
• Pregnant or high skin temperature

St. Louis Encephalitis

Eastern Equine Encephalitis

LaCrosse Encephalitis

West Nile Virus, 2016

CA, 2016: 3 cases reported

Eastern Equine
Encephalitis

LaCrosse
Encephalitis

West Nile Virus, 2016
Zika

Objectives

• Identify the major mosquito-borne illnesses afflicting children in the U.S. and its territories
• Discuss transmission and clinical features of Zika virus infection
• Present evolving recommendations about Zika for primary care clinicians
• Discuss Zika treatment and prevention strategies

What is Zika?

• Flavivirus, closely related to dengue, yellow fever, and West Nile viruses
• First isolated in 1947 in Zika Forest (Uganda)
• Monkeys were primary host
• Prior to 2007, only rare cases of “spillover infections” into humans

Human Infection with Zika Virus

1947:
Virus first isolated from Uganda (Zika Forest)
1952:
First human case reported
2007:
First outbreak Micronesia (Yap Island)
2013:
Outbreak in French Polynesia
2016:
Throughout Americas/Caribbean

June 2016:
First locally acquired case in Brazil
May 2015:
First locally acquired case in Brazil
Dec 2015:
1.3 million cases in Brazil

December 2015:
1.3 million cases in Brazil

1947:
Virus first isolated from Uganda (Zika Forest)
1952:
First human case reported
2007:
First outbreak Micronesia (Yap Island)
2013:
Outbreak in French Polynesia
2016:
Throughout Americas/Caribbean

1947:
Virus first isolated from Uganda (Zika Forest)
1952:
First human case reported
2007:
First outbreak Micronesia (Yap Island)
2013:
Outbreak in French Polynesia
2016:
Throughout Americas/Caribbean

May 2015:
First locally acquired case in Brazil

Global Zika Activity, February 2017

Zika Cautionary Areas

TRAVELERS:
- If pregnant, consider delaying travel

RESIDENTS/PAST TRAVELERS:
- If pregnant, testing recommended
- If trying to conceive, consider waiting 8+ weeks after symptoms or last exposure (woman)
- Use condom x 6 months after symptoms or last exposure

Theories on How Zika Was Introduced into Brazil

- Spring, 2014: World Cup in Brazil
- August, 2014: Va’a canoe event in Rio de Janeiro
  – included participants from French Polynesia
- June, 2013: Confederation Cups soccer tournament
  – Phylogenetic analyses suggest single introduction of Zika virus May-Dec 2013

Why has Zika emerged now?

- Naive populations in South Pacific amplified virus and facilitated spread via global mobility
- Abundance of competent vectors in the Americas
- Mutational changes
  - enhanced viral infectivity of Aedes vectors
  - enhanced human viremia and improved transmission efficiency

Why this explosive spread?

- Naive populations in South Pacific amplified virus and facilitated spread via global mobility
- Abundance of competent vectors in the Americas
- Mutational changes
  - enhanced viral infectivity of Aedes vectors
  - enhanced human viremia and improved transmission efficiency

Zika Transmission

- Transmitted primarily by Aedes spp. mosquitoes
  - Breed in domestic water containers
  - Aggressive daytime biters
  - Prefer humans
  - Also transmit dengue and chikungunya

Theories on How Zika Was Introduced into Brazil

- Spring, 2014: World Cup in Brazil
- August, 2014: Va’a canoe event in Rio de Janeiro
  – included participants from French Polynesia
- June, 2013: Confederation Cups soccer tournament
  – Phylogenetic analyses suggest single introduction of Zika virus May-Dec 2013

Why has Zika emerged now?

- Naive populations in South Pacific amplified virus and facilitated spread via global mobility
- Abundance of competent vectors in the Americas
- Mutational changes
  - enhanced viral infectivity of Aedes vectors
  - enhanced human viremia and improved transmission efficiency
Other Modes of Zika Transmission

- Congenital and perinatal
- Laboratory exposure (1 case)
- Blood transfusion (from asymptomatic donors)
- Organ transplantation
- Bodily fluids (urine, saliva, blood, tears, vaginal secretions, semen)

➢ Virus present in breast milk but no evidence of transmission

Sexual Transmission of Zika

- Salivary and semen isolates sequenced and virtually identical upon phylogenetic analysis.

Is Zika an STI?

- Prolonged shedding in semen and vaginal secretions
  - Semen sample
    • Zika RNA detected 80+ days after symptom onset (188 days reported).
    • Male-to-male and male-to-female transmission
  - Vaginal secretions
    • Zika RNA: Up to 23 days
    • Only one case of female-to-male transmission reported
  - Blood
    • Zika RNA: 8-13 days

CLINICAL MANIFESTATIONS
Confirmed Zika Virus Disease, Yap Island (2007)

- Infection rate 73%*
- Incubation period 5-14 days
- Symptomatic attack rate 18%
- All age groups affected
- Children more likely to have subclinical disease
- No severe disease, hospitalizations, or deaths

*Symptoms

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>#: (% of 313)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maculopapular rash</td>
<td>28 (90%)</td>
</tr>
<tr>
<td>Sore joints</td>
<td>20 (65%)</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>16 (55%)</td>
</tr>
<tr>
<td>Conjunctivitis</td>
<td>17 (52%)</td>
</tr>
<tr>
<td>Myalgia</td>
<td>15 (48%)</td>
</tr>
<tr>
<td>Headache</td>
<td>14 (45%)</td>
</tr>
<tr>
<td>Retro-orbital pain</td>
<td>12 (38%)</td>
</tr>
<tr>
<td>Edema</td>
<td>6 (19%)</td>
</tr>
<tr>
<td>Somnolence</td>
<td>3 (10%)</td>
</tr>
</tbody>
</table>

Based on random sample of 173 households, 557 people > 3 yrs

Zika and Microcephaly

- October 2015; Pernambuco, Brazil
  - Increased number of neonates with microcephaly reported
  - No common teratogenic exposures
  - Majority of mothers reported rash illness early in pregnancy

Zika and Microcephaly, early evidence

- Obstetric clinic-based cohort study in Brazil
  - 88 pregnant women with recent rash illness (onset ≤ 5 days)
  - 5-38 wks EGA at enrollment
  - 72 (88%) had Zika detected in urine and/or blood
  - Fetal abnormalities detected in ≈30% of Zika-infected women who underwent fetal ultrasound
  - No fetal abnormalities detected in Zika-negative women

- National active surveillance study in Columbia
  - 4 infants with microcephaly born to women without symptoms
  - All had evidence of congenital Zika

Zika and Microcephaly

- October 2015; Pernambuco, Brazil
  - Increased number of neonates with microcephaly reported
  - No common teratogenic exposures
  - Majority of mothers reported rash illness early in pregnancy

Pregnancy Outcomes--Bahia, Brazil (June, 2016)

- Fetal ultrasound of 42 pregnant women with confirmed Zika infection
  - 28% with abnormalities

- Hydrocephaly
- Calcifications
- Microcephaly
- Fetal death
Pregnancy Outcomes—Bahia, Brazil (December, 2016)

- Fetal deaths: 7.2% (9 of 125)
- Fetal/neonatal abnormalities: 42% (49 of 116)

Confirmed Zika Virus Disease, French Polynesia (2013-2014)

Association between Zika virus and microcephaly in French Polynesia, 2013-15: a retrospective study

Summary

Background: The emergence of Zika virus in the Americas has coincided with increased reports of babies born with microcephaly in many countries. Studies have suggested that the risk of microcephaly is highest in infants infected in the first trimester of pregnancy.

Methods: We retrospectively analysed data from a Zika virus outbreak in French Polynesia, which was the largest documented outbreaks before the Americas. We used epidemiological and surveillance data to estimate the probability of infection with Zika virus in each week of the pregnancy, and maternal and newborn records in order to assess all cases of microcephaly, stillbirth, and congenital anomalies. We used standardised incidence ratios to estimate periods of risk in the first trimester of pregnancy.

Findings: The Zika virus outbreak began in November 2013, and ended in April 2015, and 140 (95% CI 125-156) of the 543 women who provided medical records in the time period October 2013 to April 2015 had microcephaly. In the time period before the Zika outbreak began, before March 2013, there were 9 cases of microcephaly among 516 women (1.7%), while in the outbreak period, from November 2013 to April 2015, 12 cases of microcephaly were noted, an increase of 79% (1.7% vs 3.1%) (P = 0.07). The probability of Zika virus infection in each week of pregnancy was highest in the first trimester (odds ratio 2.2, 95% CI 1.3 to 3.6). Of the 12 cases of microcephaly noted in the outbreak period, 5 cases (42%) were in infants born to women infected during the first trimester of pregnancy.

Strengths and Limitations: The study was limited by the absence of information on the menstrual cycles of women diagnosed as having Zika virus infection. The outbreak was also limited to French Polynesia, which is a small Pacific island nation.

Fetal Brain Disruption Sequence

- Collapse of fetal skull following destruction of brain tissue
- Severe microcephaly: HC < 3rd percentile
- Cerebral calcifications, cortical malformation, ventriculomegaly

Confirmed Zika Virus Disease, French Polynesia (2013-2014)

Association between Zika virus and microcephaly in French Polynesia, 2013-15: a retrospective study

Summary

Background: The emergence of Zika virus in the Americas has coincided with increased reports of babies born with microcephaly in many countries. Studies have suggested that the risk of microcephaly is highest in infants infected in the first trimester of pregnancy.

Methods: We retrospectively analysed data from a Zika virus outbreak in French Polynesia, which was the largest documented outbreaks before the Americas. We used epidemiological and surveillance data to estimate the probability of infection with Zika virus in each week of the pregnancy, and maternal and newborn records in order to assess all cases of microcephaly, stillbirth, and congenital anomalies. We used standardised incidence ratios to estimate periods of risk in the first trimester of pregnancy.

Findings: The Zika virus outbreak began in November 2013, and ended in April 2015, and 140 (95% CI 125-156) of the 543 women who provided medical records in the time period October 2013 to April 2015 had microcephaly. In the time period before the Zika outbreak began, before March 2013, there were 9 cases of microcephaly among 516 women (1.7%), while in the outbreak period, from November 2013 to April 2015, 12 cases of microcephaly were noted, an increase of 79% (1.7% vs 3.1%) (P = 0.07). The probability of Zika virus infection in each week of pregnancy was highest in the first trimester (odds ratio 2.2, 95% CI 1.3 to 3.6). Of the 12 cases of microcephaly noted in the outbreak period, 5 cases (42%) were in infants born to women infected during the first trimester of pregnancy.

Strengths and Limitations: The study was limited by the absence of information on the menstrual cycles of women diagnosed as having Zika virus infection. The outbreak was also limited to French Polynesia, which is a small Pacific island nation.

Fetal Brain Disruption Sequence

- Collapse of fetal skull following destruction of brain tissue
- Severe microcephaly: HC < 3rd percentile
- Cerebral calcifications, cortical malformation, ventriculomegaly

Neuroimaging and Congenital Zika

- Craniofacial disproportion
- Corpus callosum hypoplasia
- Massive hydrocephaly
- Calcifications
- Over-riding bones, excess skin
**Neurotropism and Zika**

- Shepard’s Criteria
  - Rare exposure and rare outcome tightly associated
    - Zika PCR+ in 30/31 neonates with microcephaly
  - Specific clinical syndrome
  - Exposure at time of developmental vulnerability
  - Makes biological sense

Zika infects neural crest cells (red) using AXL receptor for entry (green).

However, also infects mature neural cells.

- Rasmussen, NEJM, 2016.
- Cordeiro, EID, 2016.

---

**Zika in Pregnant Women**

<table>
<thead>
<tr>
<th>Total Cases</th>
<th>U.S.</th>
<th>U.S. Territories</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pregnancy Outcomes</td>
<td>3,071</td>
<td>3,071</td>
</tr>
</tbody>
</table>

- Liveborn with birth defect: 38 (2.7%)
- Pregnancy loss with birth defect: 5 (0.4%)

---

**Current Burden (February, 2017)**

<table>
<thead>
<tr>
<th></th>
<th>U.S.</th>
<th>U.S. Territories</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Cases</td>
<td>5,001</td>
<td>36,498</td>
</tr>
<tr>
<td>Travel-associated</td>
<td>4,780</td>
<td>140</td>
</tr>
<tr>
<td>Sexual transmission</td>
<td>41</td>
<td>?</td>
</tr>
<tr>
<td>Lab-acquired</td>
<td>1</td>
<td>?</td>
</tr>
<tr>
<td>Locally-acquired, mosquito-transmitted</td>
<td>220</td>
<td></td>
</tr>
<tr>
<td>Guillain Barre syndrome</td>
<td>13</td>
<td>51</td>
</tr>
</tbody>
</table>

---

**Why Such Different Rates??**

- Timing of exposure
  - In US cohort
    - 1st trimester risk = 11% vs 2nd-3rd trimester risk = 0%
- Intensity of exposure
  - Over time
- Reporting bias
  - Under vs. over ascertainment of asymptomatic pregnant women??

---

**Zika Virus Infection in Pregnant Women in Rio de Janeiro**

<table>
<thead>
<tr>
<th>125 Zika+</th>
<th>61 Zika-</th>
</tr>
</thead>
<tbody>
<tr>
<td>127 (93%) live births</td>
<td>57 (92%) live births</td>
</tr>
<tr>
<td>40 (42%) imaging/exam abnl</td>
<td>3 (5%) imaging/exam abnl</td>
</tr>
<tr>
<td>11 (17%) fetal deaths</td>
<td>4 (7%) fetal deaths</td>
</tr>
</tbody>
</table>
Think Zika!

- In U.S., 47 live-borne infants with birth defects and 5 pregnancy losses with birth defects (of 1,143 completed pregnancies of Zika + women in US)
- Any infant with microcephaly, intracranial calcifications and/or eye abnormalities*
- Neonate with rash, fever, conjunctivitis — born to mother who traveled to endemic region within 2 wks of delivery OR has a partner who has traveled to endemic region within prior 6 months.

*Including macular atrophy, optic nerve alterations, optic disc hypoplasia, gross macular pigment mottling


Measuring Head Circumference For Microcephaly

- Optimal measurement within 24 hours after birth.
- Use a measuring tape that cannot be stretched
- Take the measurement three times and select the largest measurement to the nearest 0.1 cm

- Securely wrap the tape around the widest possible circumference of the head — Broadest part of the forehead above eyebrow — Above the ears — Most prominent part of the back of the head


Case Definition of Microcephaly

Definite congenital microcephaly for live births

- Head circumference (HC) at birth is less than the 3rd percentile for gestational age and sex.
- If HC at birth is not available, HC less than the 3rd percentile for age and sex within the first 6 weeks of life.

Congenital Zika: Beyond Microcephaly

The likelihood is that Zika will leave long-lasting scars on developing brains is “close to 100%”.

Zika “poses a much more serious long-term risk to the health of a generation than the more obvious microcephaly in a few infants”.

- Edwin Trevathan, MD, MPH
  [former Director, CDC National Center of Birth Defects]

Congenital Zika Virus Infection Beyond Neonatal Microcephaly

- Tropism for mature neural crest cells — Brain development continues after birth
- Abnormalities noted in infants with normal head circumferences — Craniofacial disproportion (loss of brain volume) — Spasticity, seizures — Brainstem dysfunction — Ocular abnormalities — Hearing loss — Findings on neuroimaging (calcifications, cortical disorders and ventriculomegaly)

Risks beyond 1st Trimester

- Mom infected in early 3rd trimester (16 wks)
- Normal fetal ultrasound (38 wks)
- Mild microcephaly noted at birth (other growth parameters normal)
- CSF, blood and urine + Zika
- Infant with profound delay at 6 months.
Risks beyond 1st Trimester

- Brazilian report
  - 2 women with febrile rash illness at 36 wks
  - Maternal Zika PCR + (blood and urine)
  - Infants born at 38 wks
    - Normal head circumference (35 cm, 35.5 cm)
    - Normal eye exams
    - Abnormal MRI findings:
      - Subependymal cysts
      - Lenticulostriate vasculopathy
    - Normal development at 1 and 3 months

Other non-neurologic effects

- Arthrogryposis
  - Congenital joint contractures
  - Presumed neurogenic origin
  - Involvement of central and peripheral motor neurons
  - Reduced in utero movement
  - Fixed posture → contracture

- In utero growth retardation

Clinical features

- Incubation period typically 5-10 days
  - Range 1-14 days.
  - Range 8-21 days after sexual transmission
- Clinical illness is usually mild.
  - 80% of cases are asymptomatic
  - Symptoms last several days to a week.
- Severe disease is uncommon.
  - Thrombocytopenia during convalescence (immunoenhancement due to prior dengue infection)
  - Unknown outcomes in immunocompromised patients.

Clinical symptoms and signs in 93 patients with Zika virus disease acquired in the Americas

- Guillain-Barre Syndrome
  - Immune-mediated damage to myelin sheath
  - Linked to several infectious illnesses
  - Causes an ascending weakness/paralysis
  - May begin with paresthesias
  - Typically progresses for 2-4 wks
  - Recovery may take months
Zika and Guillain-Barre Syndrome

- Association noted in prior outbreaks (French Polynesia)
- Case-control study (matching to patients hospitalized with non-febrile illness)
- Zika + IgM/IgG
  - 41 of 42 (98%) cases
  - 54 of 98 (56%) controls

Santos, NEJM, 2016.
Parra, NEJM, 2016.

Neurological and Other Complications of Zika

- Meningoencephalitis
- Acute myelitis
- Hearing loss
- Severe thrombocytopenia
  - plt<5,000/ul.
- Uveitis
- Conjunctivitis
  - Nonpurulent
  - Often with keratitis/uveitis
  - Zika in aqueous humor (by PCR)

Furtado, NEJM, 2016.
Sharp, CID, 2016
Vinhaes, CID, 2017.
Carteaux, NEJM, 2016

Objectives

- Identify the major mosquito-borne illnesses affecting children in the U.S. and its territories.
- Discuss the clinical effects of Zika virus infection.
- Present evolving recommendations about Zika for primary care clinicians.
- Discuss Zika treatment and prevention strategies.

Zika Diagnosis

- Reverse transcriptase PCR (blood, plasma, urine, saliva, CSF)
  - Highest yield day 0-7 after symptom onset
  - Whole blood PCR may remain positive longer than urine or plasma
- Zika IgM serology
  - Cross reacts with dengue → need negative dengue or 4X higher Zika titer
  - Send for neutralizing antibodies (PRNT) to confirm
- 4-fold rise titer by PRNT (acute vs. convalescent sera)
- Direct viral detection in amniotic fluid or tissue

Timing of ZIKV Diagnostics
Who to Test for Zika Virus (1)

- **Neonates**
  - Born to mother with laboratory evidence of Zika during pregnancy
  - With clinical features suggestive of Zika and epidemiologic link
- **Pregnant Women**
  - Live in or travel to Zika area (regardless of symptoms)
  - Have a sex partner who lives in or traveled to Zika area
- **Others**
  - Symptoms consistent with Zika
  - Exposure to Zika area (self or sex partner)

Zika is nationally reportable!

Who to Test for Zika Virus (2)

- **WHO NOT TO TEST:**
  - Someone who is asymptomatic (unless they are pregnant and have been exposed)
  - Someone who has been exposed and is concerned about transmitting Zika through sexual contact

- **RATIONALE:**
  - False negative rate of tests are unknown.
  - We don’t know if a negative Zika test means you cannot pass Zika to your partner.

Recommended Initial Evaluations for Infant with Congenital Zika

- **Neurologist**
  - Determine appropriate neuroimaging and evaluation
- **Ophthalmologist**
  - Comprehensive eye exam (cortical visual impairment)
- **Endocrinologist**
  - Hypothalamic or pituitary dysfunction
- **Audiology evaluation**
  - Auditory brain response (ABR) to assess hearing.
- **Infectious disease specialist**
  - Workup of other congenital infections
- **Clinical geneticist**
  - Evaluate for other causes of microcephaly

Pediatric Evaluation and Follow-up Tools


Evaluation and Follow-up Tools for Pregnant Women


Objectives

- Identify the major mosquito-borne illnesses afflicting children in the U.S. and its territories.
- Discuss the transmission and clinical features of Zika virus infection.
- Present evolving recommendations about Zika for primary care clinicians.
- Discuss Zika treatment and prevention strategies.
Guidance for Infected Patients

- **Symptomatic treatment**
  - Rest and fluids
  - Use acetaminophen to reduce fever and pain
  - Do not take aspirin or NSAIDS until dengue can be ruled out to reduce the risk of bleeding.

- **Prevent secondary spread**
  - Avoid mosquito bites while potentially infectious (viremia persists 1-7 days post symptom onset)
  - Do not donate blood
  - Men to use barrier protection if sexually active for 6+ months (even if no history of symptoms)

Strategies to Prevent Zika

- **Avoid Mosquito Exposure**
  - Keep mosquitoes out
    - Window screens, closed doors, air conditioning
  - Drain standing water
    - After rain, check around yard for pooling
  - Prevent mosquito breeding
    - Every week, drain water and scrub interior of outdoor water-containing vessels
      - Kiddie pools, bird baths, fountains, flower pots and planters

- **Restrict Travel**
  - **Who and When?**
    - Women who are pregnant, trying to conceive, or may want to conceive within 6-12 months
    - Men who are their partners
  - **Where?**
    - Use most up-to-date resources (CDC and WHO recommended)

Challenges to Prevention

- Preliminary poll results about knowledge and attitudes toward Zika
  - “Past” and “Future” travelers to Zika-affected areas
  - Only 49% of past travelers saw info about self-protection from Zika
    - If saw info then 69% felt more motivated to take precautions

Avoid Mosquito Exposure
Avoid Direct Exposure to Zika

- **Protection during sex**
  - Use condoms if partner has traveled to Zika-endemic area
  - Duration of use depends on
    - Partner developed symptoms suggestive of Zika
      - Women: 8 weeks
      - Men: 6 months
    - Men 6 months since last possible exposure if unsymptomatic
    - Pregnant
      - Duration of pregnancy

Protective Measures during Sex:

- Use condoms if partner has traveled to Zika-endemic area.
- Duration of use depends on:
  - Partner developed symptoms suggestive of Zika:
    - Women: 8 weeks
    - Men: 6 months
  - Men 6 months since last possible exposure if unsymptomatic.
  - Pregnant: Duration of pregnancy.

Prevent Mosquito Bites

- **Create barrier**
  - Clothing, netting over strollers
  - Permethrin treatment of clothing (never on skin)

- **Use an FDA-registered insect repellent**
  - DEET, picaridin, IR3535 if > 2 months
  - Oil of Lemon Eucalyptus for children older than 3 years

What Exactly is DEET?

- **“Gold Standard” — most widely used**
  - Available since 1948
  - Repels mosquitoes, ticks, fleas, midges, chiggers, black flies, most others

- **Available in concentrations from 5-100%**
  - 25%+ concentration best against Aedes mosquitoes

- **Multiple formulations available**
  - Available in sustained release products
  - Aerosols, sprays, creams, towelettes

- **Do not use on children <2 months**

Concentration and Protection Time

Protection Times Vary by:

- Gender
- Activity
- Washes off with perspiration
- Time of day
- Weather
- Temperature, humidity, wind
- How much CO₂/other attractants you emit

Other Options

**Picaridin and IR3535**
- Must be 2+ months of age
- Repel mosquitoes, biting flies, ticks, fleas, and chiggers
- Introduced in US in 2005 and 2000, respectively
- IR3535 not available in wipe form

**Lemon Eucalyptus Oil**
- Must be 3+ years of age
  - Essential oils can cause skin irritation
  - Repel mosquitoes, flies, gnats, ticks
  - Available since 2000

Protection for Pregnant Women and Nursing Mothers

- EPA-registered products have been tested for safety and efficacy

- Use of DEET-based products recommended by
  - CDC
  - WHO
  - American Academy of Pediatrics
  - American College of Obstetrics and Gynecology

- Study in Thailand showed no issues with moms or children
**How to Use**

- Apply sparingly
- Apply sunscreen before repellent
- Cover all exposed skin surfaces
- Smooth on like lotion
- Apply to hands and then face
- Spray lightly onto clothing
- Don’t spray a cloud and walk through it
- Reapply repellent when bugs return
- Higher concentration = longer protection

**Blood Safety**

- **August 26th, 2016:**
  - Screening donated blood for Zika nucleic acid under IND assay (FL, TX, SC, AL, MS, GA)*
  - Screening donors by questionnaire (all states)
    - Medical diagnosis of Zika in past 6 months.
    - Residence in, or travel to, an area with active ZIKV transmission in past 6 months.
    - Sex in past 6 months with a male who is known to have either of the risk factors.

*To be adopted within 6 wks by states with large numbers of travelers from Zika-endemic settings.

**Vaccine Development Strategy**

- **Evaluate** promising candidates during highest disease incidence (2016 - 2017)
- **Deploy** a vaccine(s) for use during the ongoing epidemic to protect populations at highest risk (2018 - 2019)
- **Commercialize** a vaccine(s) to reduce the disease burden in the general population (2020)

**Zika Vaccine Landscape**

- Two DNA vaccines completed Phase 1
  - Phase 2 started June in Puerto Rico for one
  - Phase 2 starting Jan 2017 for the other
- Whole inactivated vaccine with alum Phase 1 starting soon
- Target populations:
  - Women of reproductive age and their partners
  - Travelers
  - CSWs in endemic areas
Novel Prevention Strategies

**Wolbachia pipientis**
- Bacteria that infects variety of insects
- Asymptomatic infection, but...
- Associated with reduced frequency and titer of Zika virus in saliva of mosquitoes
- Vertical passage (progeny also infected)
- Also inhibits dengue virus

What’s RIDL?
*Release of Insects with Dominant Lethality*
- Genetically engineered male mosquitoes
  - Carry lethal gene that results in premature death of progeny
- Rapid reductions in insect burden
- Theoretical Benefits:
  - No short-term increase in risk (only females bite)
  - Species-specific (reduced impact on other organisms)
  - May be more cost-effective than other vector control strategies

Summary
- Zika is a major threat to the public’s health although infection of non-pregnant individuals is relatively minor.
- Repercussions of this outbreak will be felt for generations.
- Human behavior and environmental management are essential to limit spread.

Additional Resources
DEET Urban Legends

- Causes seizures
  - Extensive independent reviews show this is not true
- Higher concentrations are more dangerous
  - No relationship between adverse events and concentration
- Children are at greater risk
  - Adverse events not related to age
- Causes death
  - Use according to directions is NOT a problem
  - Deaths from ingestion of large amounts
  - Suicides

Bibliography