Zika in Travelers: the GeoSentinel Experience

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GeoSentinel (CDC/ISTM)
GeoSentinel Surveillance System Overview

Established in 1995 by CDC and International Society for Travel Medicine (ISTM)

Clinic-based global surveillance system
- International travelers and immigrants
- De-identified patient information
- Central electronic database
- Link time and place of exposure
- Monitor disease burden and distribution
- Detect new infections and patterns

Currently co-funded by CDC (DGMQ), ISTM, and PHAC
Sites Contributing Data

64 GeoSentinel sites:

- 24 North America
- 22 Europe
- 9 South and SE Asia
- 2 South America
- 2 Australia / New Zealand
- 3 Africa
- 2 Middle East
GeoSentinel Zika in the Americas Analysis

Cases entered by all sites between Jan 1, 2013 and Feb 29, 2016

Limited to patients who had traveled to the Americas

Standard GeoSentinel data collected plus supplemental information on exact destinations, symptoms and laboratory testing

– Hamer DH et al. Ann Int Med 2017
Zika Diagnostic Criteria

Clinical criteria (S): 1 or more of following:

- Fever, rash, arthralgia, conjunctivitis, pregnancy complication, Guillain-Barré syndrome

Probable case (P):

- Clinical criteria plus travel to area with Zika transmission
- Direct epidemiological linkage to person with Zika (e.g. sexual contact, *in utero* transmission
- AND positive ZIKV-specific IgM in serum or CSF
- Negative dengue-specific IgM and no neutralizing Ab testing or <4X difference with Zika titer
Zika Diagnostic Criteria – Confirmed Case (C)

- Meets clinical criteria AND
- Lab evidence of recent ZIKV infection by:
  - Detection ZIKV by PCR, culture, or viral Ag in serum, CSF, tissue or other specimen
  - ZIKV IgM antibodies in serum or CSF with ZIKV neutralizing antibody titers 4X or greater than titers for dengue or other locally endemic flaviviruses

Council of State and Territorial Epidemiologists, revised February 2016
Month of clinic visit for 93 Zika-infected patients evaluated at GeoSentinel sites
GeoSentinel Zika in Americas: Results

- 93 patients: 62% women
  - 69% confirmed; 14% probable; 17% suspect

- Age distribution: mean 41 y, range 3-77 y

- Reason for travel: 48% tourism; 40% VFR; 8% business

- 96% of patients managed as outpatients

- Sentinel case: Costa Rica, Danish traveler
  - Chen LH. Ann Int Med 2016
Travel Routes and Zika Exportation
March 2015 – February 2016
Region/Country of Exposure*

- **South America:** 59%
  - Suriname, Colombia, Brazil, Venezuela

- **Caribbean:** 24%
  - Martinique, Haiti, DR, Guadeloupe, Dutch Antilles

- **Central America and Mexico:** 16%
  - Honduras, Mexico, Costa Rica, El Salvador

*More than one region and country of exposure possible*
### Symptoms at Presentation to GeoSentinel Site (n = 93)

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Percent of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exanthema</td>
<td>88%</td>
</tr>
<tr>
<td>Fever</td>
<td>76%</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>72%</td>
</tr>
<tr>
<td>Headache</td>
<td>61%</td>
</tr>
<tr>
<td>Myalgia</td>
<td>60%</td>
</tr>
<tr>
<td>Other*</td>
<td>49%</td>
</tr>
<tr>
<td>Fatigue</td>
<td>47%</td>
</tr>
<tr>
<td>Conjunctivitis</td>
<td>40%</td>
</tr>
<tr>
<td>Pruritus**</td>
<td>23%</td>
</tr>
</tbody>
</table>

**Percent of Patients**

![Bar chart showing the percentage of patients with each symptom]
Other, Unusual Symptoms & Complications

- Severe itching, nausea, diarrhea, anorexia, loss of taste, tingling
- Guillain-Barré syndrome (2 patients)
- Elective pregnancy termination
  - Fetal US: microcephaly, large ventricles, and agenesis of corpus collosum
- Thrombocytopenia: 10K with bruising  
Hematological Data

- Median WBC count (n = 83):
  - 5500 cells/mL (range: 2600 - 14,500)

- Hemoglobin (n = 82):
  - 13.4 g/dL (range: 7 - 16.2)

- Platelet count (n = 84):
  - 218,500 per mL (range: 10,000 - 515,000)
Conclusions

• Substantial regional variation in diagnostic testing for Zika
• GeoSentinel data not necessarily representative of all travelers
• Assumed vector-borne transmission for all infected travelers
Confirmed Zika from the Americas from October 2015 to December 2016
Zika in SE Asia, South Pacific and Africa: GeoSentinel Analysis

- Database reviewed for reported Zika cases from 1995 to December 2016
- Cases classified using modified CSTE definitions – confirmed and probable
- Comprehensive search of PubMed, ProMED and other outbreak sites to identify reported cases and timing of reporting
GeoSentinel Reports of Zika in Travelers Outside of the Americas

- First reported case of Zika virus infection occurred in traveler to Indonesia in May 2012
  - Cameroon traveler from 2010 retrospectively identified
- 2 cases reported in 2013, 5 in 2014, 3 in 2015, and 13 in 2016
- 14 cases acquired in SE Asia, 9 in the Pacific, and one in Africa
- 19 confirmed; 5 probable
Zika Countries of Exposure and Diagnosis
Patient and Trip Characteristics

- 14 males and 10 females
- Median age 41 years (range: 20-66 y)
- Most common purpose of travel was tourism (46%), migrant labor (17%), VFR (13%) and missionary (13%)
- Median duration of travel to exposure 17 days (range 7-335 d)
- Median time symptom onset to clinic presentation 6 d (2-35 d)
Possible Sentinel Cases

- **2012**: Indonesia (diagnosed in Australia)
  - Kwong JC et al. AJTMH 2013

- **2014**: the Philippines (dx in Germany)
  - First case since 2012 for this country

- **2013**: Thailand (dx in Canada)
  - Serological data in Thailand from the 1950s
    - Fonseca C et al. AJTMH 2014

- **2015**: Vietnam (dx in Israel)
  - Serological data in Vietnam from the 1950s
Sentinel Cases

2010: Cameroon (diagnosed retrospectively in Belgium)
  - Only reported case in Cameroon since 2010

2015: Kirabati (dx in New Zealand)
  - First known report

April 2016: East Timor (dx in Germany)
  - First known report although only probable
Figure 2. Map of Asian countries in which Zika virus circulation has been reported up to September 1, 2016.
Conclusions

- Travelers may serve as sentinels of local Zika transmission and potentially impending outbreaks
- Sentinel surveillance can complement local surveillance activities
- Travelers represent potential source for local introduction (if competent vector) or through sexual transmission
- Sentinel surveillance data can be used by international authorities for country risk categorization
Acknowledgments

Site directors and co-directors

GeoSentinel leadership team

CDC team

ISTM administrative team

Special advisors

Funding from CDC (U50CK00189), ISTM and PHAC