GeoSentinel: A Surveillance Network of Returning Travelers and Migrants

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Disclosures

• GeoSentinel funding from US CDC, ISTM and PHAC
• Consulting fees: iJET, Valneva
• Speaking honorarium: Merck
Talk Outline

• Description of GeoSentinel
• Analysis of ill travelers (2007 – 2011)
• GeoSentinel Zika analyses
• Examples of outbreak reports
GeoSentinel Surveillance Network Overview

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

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

Co-funded by CDC (DGMQ), ISTM, and PHAC
### Variables Collected in GeoSentinel

<table>
<thead>
<tr>
<th>Demographics</th>
<th>Travel History</th>
<th>Clinical Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>Recent travel history</td>
<td>Inpatient/outpatient</td>
</tr>
<tr>
<td>Age</td>
<td>Previous travel history</td>
<td>Main presenting symptoms</td>
</tr>
<tr>
<td>Country</td>
<td>Country or countries of exposure to current illness</td>
<td>Underlying conditions</td>
</tr>
<tr>
<td>Birth</td>
<td>Reason for travel related to current illness</td>
<td>Diagnosis</td>
</tr>
<tr>
<td>Citizenship</td>
<td>Seen during travel, after travel or after immigration</td>
<td>Diagnostic method(s)</td>
</tr>
<tr>
<td>Residence before age 10</td>
<td></td>
<td>Diagnosis status (confirmed/probable)</td>
</tr>
<tr>
<td>Current residence</td>
<td></td>
<td>Antibiotic susceptibility data (for 9 select pathogens)</td>
</tr>
<tr>
<td>History of immigration</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-travel encounter with a healthcare provider</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
How does GeoSentinel work?

Patients with travel-related condition

GeoSentinel Site or Affiliate Members

Surveillance Data

Central Database

Reports

Data analysis by Sites

Rapid Query Response Loop

GeoS Sites and Affiliate Members +/- ISTM Membership +/- Partners (e.g. TropNet, PHAC, ProMED, and Healthmap)
Sentinel Sites Contributing Data
(as of February 20, 2018)

70 GeoSentinel sites in 31 countries:
- 27 North America
- 25 Europe
- 10 SE and South Asia
- 3 South America
- 2 Australia / New Zealand
- 2 Africa
- 1 Middle East

215 Affiliate members
GeoSentinel Sites
(dots = sites; shaded areas = affiliate members)
Affiliate Members: Benefits

• Accelerated acquisition of alerts & advisories on breaking events from GeoSentinel
• Routine reporting not required
• Recognition of individuals reporting a key sentinel event in the press, ProMed, ISTM NewsShare, and public health bulletins
• Potential participation in outbreak reports
• Access to members-only section of the GeoSentinel website
Data Summary

Numbers of patient encounters:
• 304,404 patients total
• 385,172 final diagnoses
  as of 30 January 2018

GeoS records cover traveler, immigrant, and refugee exposures in 251 countries and territories
GeoSentinel Contributions as of January 2018

Europe: 37%
Nepal (Katmandu): 16%
US: 14%
Canada: 11%
Asia: 11%
Mexico: 1%
S. America & Africa: 4%
Israel: 3%
Oceana: 3%
Who are GeoSentinel Patients? (as of January 2018)

Complete Database

After Travel Visits Only (~57%)

- **Tourists**: 62%
- **VFR**: 14%
- **Mission, Volunteer, Research**: 10%
- **Business**: 11%
- **Student, medical tourism, military**: 3%

- **Visit Clinic After Travel**: 57%
- **Visit Clinic During Travel**: 29%
- **Immigration Travel Only**: 14%
## Top 10 Diagnoses: Travelers (Previous 2 Years)

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Number of Diagnosis</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>DIARRHEA, ACUTE UNSPECIFIED</td>
<td>4137</td>
<td>12.3%</td>
</tr>
<tr>
<td>RESPIRATORY INFECTION, ACUTE</td>
<td>3515</td>
<td>10.4%</td>
</tr>
<tr>
<td>DIARRHEA ACUTE BACTERIAL</td>
<td>1956</td>
<td>5.8%</td>
</tr>
<tr>
<td>DIARRHEA, CHRONIC</td>
<td>1831</td>
<td>5.4%</td>
</tr>
<tr>
<td>VIRAL SYNDROME (WITH/WITHOUT RASH)</td>
<td>1589</td>
<td>4.7%</td>
</tr>
<tr>
<td>ZIKA (includes screening)</td>
<td>1495</td>
<td>4.4%</td>
</tr>
<tr>
<td>DENGUE, UNCOMPLICATED</td>
<td>1183</td>
<td>3.5%</td>
</tr>
<tr>
<td>DIARRHEA ACUTE parasitic</td>
<td>1148</td>
<td>3.4%</td>
</tr>
<tr>
<td>BITE, ANIMAL</td>
<td>1122</td>
<td>3.3%</td>
</tr>
<tr>
<td>MALARIA (ALL SPECIES)</td>
<td>1067</td>
<td>3.2%</td>
</tr>
</tbody>
</table>
## Top 10 Diagnoses: Immigrants & VFRs (Previous 2 Years)

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Number of Diagnosis</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>AGAS DISEASE, CHRONIC</td>
<td>170</td>
<td>19.6</td>
</tr>
<tr>
<td>TUBERCULOSIS, POSITIVE IFN-RELEASE ASSAY (e.g. Quantiferon or T-SPOT) (NOT ACTIVE DISEASE)</td>
<td>97</td>
<td>11.2</td>
</tr>
<tr>
<td>M. INTESTINAL INFECTIONS</td>
<td>95</td>
<td>10.9</td>
</tr>
<tr>
<td>HISTOSOMIASIS</td>
<td>70</td>
<td>8.1</td>
</tr>
<tr>
<td>COBACTERIUM TUBERCULOSIS</td>
<td>69</td>
<td>7.9</td>
</tr>
<tr>
<td>SINOPHILIA</td>
<td>63</td>
<td>7.2</td>
</tr>
<tr>
<td>PATITIS (VIRAL- CHRONIC)</td>
<td>49</td>
<td>5.6</td>
</tr>
<tr>
<td>DS, HIV, SYPHILIS, GONORRHEA</td>
<td>25</td>
<td>2.9</td>
</tr>
<tr>
<td>HINOCOCOSIS</td>
<td>18</td>
<td>2.1</td>
</tr>
<tr>
<td>ARRHEA ACUTE parasitic</td>
<td>17</td>
<td>2.0</td>
</tr>
</tbody>
</table>
### Core Function – “ALERTS”

<table>
<thead>
<tr>
<th>Date</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>16 February 2018</td>
<td>ALERT - Media report of a yellow fever death in a Chilean tourist who visited Ilha Grande</td>
</tr>
<tr>
<td>14 February 2018</td>
<td>ALERT - GeoSentinel Yellow Fever cases - France ex Brazil, The Netherlands ex Brazil</td>
</tr>
<tr>
<td>08 February 2018</td>
<td>ALERT - Measles in Calgary ex Kolkata in a 1-year old VFR traveler</td>
</tr>
<tr>
<td>23 January 2018</td>
<td>ALERT - Acute Hepatitis E ex South Sudan</td>
</tr>
<tr>
<td>19 January 2018</td>
<td>ALERT - Measles ex Djibouti</td>
</tr>
<tr>
<td>18 January 2018</td>
<td>ALERT - Trypanosoma brucei rhodesiense ex Zambia (South Luangwa National Park)</td>
</tr>
<tr>
<td>21 November 2017</td>
<td>ALERT - Diphtheria in the Americas – 2017</td>
</tr>
<tr>
<td>05 October 2017</td>
<td>ALERT - Plague in Madagascar</td>
</tr>
<tr>
<td>21 September 2017</td>
<td>ALERT - Locally Transmitted Plasmodium falciparum and P. vivax Malaria Cases in Southern Europe</td>
</tr>
<tr>
<td>08 Sept 2017</td>
<td>CASE REPORT - Fatal cryptic case of malaria in a 4-year old Italian child</td>
</tr>
<tr>
<td>18 July 2017</td>
<td>ALERT: Non-tuberculous mycobacteria infections among medical tourists to the Dominican Republic</td>
</tr>
<tr>
<td>11 July 2017</td>
<td>ALERT - Increased hantavirus transmission in parts of Central, Eastern, and South-eastern Europe</td>
</tr>
</tbody>
</table>
Strengths of GeoSentinel

- Physician-confirmed diagnoses
- Network sites include many top tropical medicine sites and investigators
- Geographic coverage
- Ability to identify sentinel events (new foci of emerging infections)
- Capacity to describe characteristics of specific diseases among travelers
  - Country of exposure, timing, etc.
Objectives:

• To describe typical diseases in returned travelers according to region, travel reason, and patient demographic characteristics

• To describe pattern of low-frequency travel-associated diseases

• To refine key messages for care before and after travel
Results – 2007-2011 Returning Travelers

- 42,173 ill returned travelers
  - Asia (32.6%) and sub-Saharan Africa (26.7%)
- Illnesses: GI (34.0%), fever (23.3%), and dermatologic (19.5%)
- Only 40.5% reported pre-travel medical visits
- Relative frequency of many diseases varied with both travel destination and reason for travel
Top identified specific causes for GI, fever, dermatologic, and respiratory illnesses by region among ill returned travellers

Sub-Saharan Africa (n = 11 251)
- Gastrointestinal
  - Giardia
  - Strongyloides
  - Campylobacter
  - Salmonella
  - Shigella
  - Febrile (n = 4222)
  - P. falciparum
  - Rickettsia, SF
  - Dengue
  - P. vivax
  - Enteric fever
- Dermatologic (n = 1731)
  - CLM
  - Rabies PEP
  - Myiasis
  - Tungiasis
  - Scabies

Latin America and Caribbean (n = 8099)
- Gastrointestinal
  - Giardia
  - Strongyloides
  - Campylobacter
  - D. fragilis
  - E. histolytica
  - Febrile (n = 1436)
  - Dengue
  - P. vivax
  - Enteric fever
  - P. falciparum
  - Hepatitis A
- Dermatologic (n = 2435)
  - CLM
  - Cutaneous leishmaniasis
  - Rabies PEP
  - Myiasis
  - Scabies
- Respiratory (n = 689)
  - Influenza
  - Pulmonary TB
  - Legionella
  - Pertussis

Southeast Asia (n = 6890)
- Gastrointestinal (n = 2038)
  - Campylobacter
  - Giardia
  - Salmonella
  - Strongyloides
  - D. fragilis
  - Febrile (n = 1818)
    - Dengue
    - P. falciparum
    - P. vivax
    - Chikungunya
    - Enteric fever
    - Leprosy
- Dermatologic (n = 226)
  - CLM
  - Scabies
  - Marine envenomation
  - Gastrointestinal
    - Influenza
    - Pulmonary TB
    - Streptococcal pharyngitis
    - Atypical mycobacteria
    - Legionella
    - Pertussis
Top 10 specific diagnoses, by main reasons for travel:

- CLM
- Campylobacter
- Dengue
- Enteric fever
- Giardia
- *P. falciparum*
- *P. vivax*
- Schistosomiasis
- Strongyloides
- TB (pulmonary or other)
Zika and the Americas

GOING TO THE CARIBBEAN?

MOSQUITOES spread diseases such as CHIKUNGUNYA and DENGUE.

Protect yourself by preventing mosquito bites.

Mosquitoes bite during the day and night.

DON'T LET MOSQUITOES RUIN YOUR TRIP.

For more information: call 800-CDC-INFO (232-4636) or visit www.cdc.gov/travel.
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
Month of clinic visit for 93 Zika-infected patients evaluated at GeoSentinel sites

Frequency

Month of Diagnosis

- May-15: 1
- Jun-15: 0
- Jul-15: 0
- Aug-15: 0
- Sep-15: 0
- Oct-15: 0
- Nov-15: 2
- Dec-15: 20
- Jan-16: 30
- Feb-16: 38
GeoSentinel Zika in Americas: Results

- 93 patients: 62% women
  - 69% confirmed; 14% probable; 17% clinically 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 cases: Costa Rica, Danish traveler
  - Chen LH. Ann Int Med 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 Time of Presentation to GeoSentinel Site (n = 93)

**Figure 2.** Clinical symptoms and signs among 93 patients diagnosed with Zika virus disease acquired in the Americas.

<table>
<thead>
<tr>
<th>Symptom</th>
<th>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>

* 46 persons reported a total of 71 additional symptoms and signs in the form of comments in this category. Those observed in ≥3 patients included diarrhea (12%), joint swelling/arthritis (9%), abdominal pain (8%), nausea (6%), anorexia (4%), retro-orbital pain (3%), pharyngitis (3%), and dysgeusia (3%).
Conclusions

- Substantial regional variation in diagnostic testing for Zika
- Symptom data in travelers similar to case series from outbreak countries
- Assumed vector-borne transmission for all infected travelers
RESEARCH ARTICLE

Zika beyond the Americas: Travelers as sentinels of Zika virus transmission. A GeoSentinel analysis, 2012 to 2016.

Karin Leder¹,²*, Martin P. Grobusch³, Philippe Gautret⁴, Lin H. Chen⁵,⁶, Susan Kuhn Lian Lim⁸,⁹, Johnnie Yates¹⁰, Anne E. McCarthy¹¹,¹², Camilla Rothe¹³, Yasuyuki Katō⁴, Emmanuel Bottieau¹⁵, Kristina Huber¹⁶, Eli Schwartz¹⁷,¹⁸, William Stauffer¹⁹, Denis Malvy²⁰, Marc T. M. Shaw²¹, Christophe Rapp²², Lucille Blumberg²³, Mogens Jensenius²⁴, Perry J. J. van Genderen²⁵, Davidson H. Hamer²⁶,²⁷, for the GeoSentinel Surveillance Network"
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
Zika Countries of Exposure and Diagnosis
Possible Sentinel Cases

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

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

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

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

- **April 2016: East Timor** (dx in Germany)
  - First known report (diagnosis - probable)
Conclusions

• Travelers may serve as sentinels of local Zika transmission and potentially impending outbreaks

• 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
Local and International Implications of Chistosomiasis Acquired in Corsica, France

Philippe Gautret, Frank P. Mockenhaupt, Frank von Sonnenburg, Camilla Rothe, Michael Libman, Kristina Van De Winkel, Emmanuel Bottieau, Martin P. Grobusch, Davidson H. Hamer, Douglas H. Esposito, Philippe Parola, Patricia Schlagenhauf, for the GeoSentinel Surveillance Network¹

Emerging Infectious Diseases • www.cdc.gov/eid • Vol. 21, No. 10, October 2015
Schistosomiasis in Corsica

- Total of 11 patients identified at GeoSentinel sites and an affiliate member
- Most met definition of suspected or probable case
  - One confirmed with positive urine O&P and a second with dual serologies
- Common source = exposure to fresh water rivers in Corsica
  - Cavu River has competent intermediate host (Bulinus spp. Snails)
### Clinical Appendix Table 1. Summary public health measures in France regarding the emergence of schistosomiasis in Corsica

<table>
<thead>
<tr>
<th>Initiated–date ended</th>
<th>Measure</th>
</tr>
</thead>
<tbody>
<tr>
<td>2014</td>
<td>Prohibition bathing in or having other contact with water from the Cavu River and urinating in certain Corsican rivers to disrupt the infection cycle</td>
</tr>
<tr>
<td>November 26, 2014</td>
<td>Serologic screening of ≈20,000 exposed persons and subsequent treatment for those who tested positive (n = 90) with praziquantel†</td>
</tr>
<tr>
<td>November 27, 2014–March 25,</td>
<td>Identification of 20 additional cases No case was acquired after exposure in 2014‡</td>
</tr>
<tr>
<td>September 2014</td>
<td>Malacologic investigation in 38 sites in Corsica (20 rivers) with identification of <em>Bulinus truncatus</em> snails in the Cavu, Solenzara, Tarcu, and Osu rivers (none was found infected with <em>Schistosoma</em> spp.)</td>
</tr>
<tr>
<td></td>
<td>Screening of cattle for <em>Schistosoma bovis</em> infection.</td>
</tr>
</tbody>
</table>

*90 local cases, 20 had parasite eggs in urine samples, 24 had urinary or gynecologic symptoms that could be attributed to schistosomiasis. The cases were in persons under 16 years of age, and many were familial clusters. Nineteen cases were in persons living in Corsica, its of Provence-Alpes-Côte d'Azur region in southern mainland France, 54 in 13 other regions of mainland France. Six cases with parasite eggs in urine.*
Yellow Fever in Travelers to Brazil

- Two sites (Rotterdam, Paris) reported (unvaccinated) patients with yellow fever acquired in Brazil—both non-fatal
  - Sao Paulo municipality (Jan 2018)
  - Brumadinho, Minas Gerais (1st week Feb 2018)

- Chilean media reports

- 3rd week of February: Bucharest site identified YF patient after travel to Rio and Ilha Grande

- 4th week of February: Swiss traveler dies from YF in Zurich (refused vaccination at pre-travel visit)
[1] Brazil case counts
[2] Chilean YF victim in Brazil
[3] Vaccination at gun point
Conclusions

• Travelers may serve as sentinels of infectious disease transmission and potentially early signals of outbreaks

• Sentinel surveillance can complement local surveillance activities

• Sentinel surveillance data can be used by international authorities to help identify specific travel-associated risks for specific countries or regions
Acknowledgments

• Site directors and co-directors
• GeoSentinel leadership team
• CDC team
• ISTM administrative team
• Special advisors
• Funding from CDC (U50CK00189), ISTM and PHAC