A Literature Review of Zika Virus

Technical Appendix

<table>
<thead>
<tr>
<th>Continent/country</th>
<th>% Seropositivity (details)</th>
<th>Years survey performed</th>
<th>Laboratory assessment method</th>
<th>Ref</th>
</tr>
</thead>
<tbody>
<tr>
<td>Africa</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kenya</td>
<td>17.6 (476/2,698 serum samples)</td>
<td>1966–1968</td>
<td>HI only</td>
<td>(74)</td>
</tr>
<tr>
<td>Nigeria†</td>
<td>a) 31.2 (59/189 by HI; 40.3 (121/300 by neutralization)</td>
<td>a) 1971–1975</td>
<td>a) HI and/or neutralization</td>
<td>(75)</td>
</tr>
<tr>
<td></td>
<td>b) 1980</td>
<td></td>
<td>b) HA and HI only</td>
<td>(76)</td>
</tr>
<tr>
<td></td>
<td>c) 1965, 1970–1971</td>
<td></td>
<td>c) HI or HI followed by neutralization</td>
<td>(77)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Côte d’Ivoire</td>
<td>47.6 (20/42)</td>
<td>1999</td>
<td>IgG by ELISA only</td>
<td>(78)</td>
</tr>
<tr>
<td>Senegal</td>
<td>6.7 (57/852)</td>
<td>1988, 1990</td>
<td>IgM by ELISA only</td>
<td>(79)</td>
</tr>
<tr>
<td>The Gambia</td>
<td>86.0 (37/43 by HI); 23.8 (10/28 by CF)</td>
<td>1979</td>
<td>HI or CF</td>
<td>(80)</td>
</tr>
<tr>
<td>Uganda†</td>
<td>a) 12 (251 patients tested)‡</td>
<td>(a) 1945–1948</td>
<td>a) Viral neutralization</td>
<td>(81)</td>
</tr>
<tr>
<td></td>
<td>b) 6.1 (8/132)</td>
<td>(b) 1984</td>
<td>b) HI only</td>
<td>(82)</td>
</tr>
<tr>
<td></td>
<td>c) 6.1 (6/99)</td>
<td>(c) Not specified</td>
<td>c) Not specified§</td>
<td>(52)</td>
</tr>
<tr>
<td>Tanzania</td>
<td>17 (36 patients tested)‡</td>
<td>1945–1948</td>
<td>Viral neutralization</td>
<td>(81)</td>
</tr>
<tr>
<td>Zambia</td>
<td>6.0 (217/3,625)</td>
<td>Unspecified</td>
<td>Unspecified†</td>
<td>(83)</td>
</tr>
<tr>
<td>Asia</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Borneo</td>
<td>44.1 (49/111)</td>
<td>1996–1997</td>
<td>“Plasma samples were tested for neutralizing antibody...sera were screened at a 1:10 dilution. Endpoint titrations were conducted for samples that tested positive (i.e., titer &gt;10).”</td>
<td>(84)</td>
</tr>
<tr>
<td>Pakistan</td>
<td>2.3 (1/43)</td>
<td>1979, 1980</td>
<td>Initial screen for antibodies (not further specified), followed by CF</td>
<td>(85)</td>
</tr>
<tr>
<td>Oceania</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yap Island,</td>
<td>74.3 (414/557)</td>
<td>2007</td>
<td>IgM by ELISA only</td>
<td>(5)</td>
</tr>
</tbody>
</table>

*Summary data of all seroprevalence surveys of Zika virus antibodies in humans, reported in peer-reviewed literature, 1952–2016. Publications for which the abstract only was accessible or that did not provide complete data were excluded. CF, complement fixation; HA, hemagglutination assay; HI, hemagglutination-inhibition; Ref, Technical Appendix reference number.
† Multiple studies were found for Nigeria and Uganda; these studies are indicated separately with a, b, c.
‡ Study for Uganda and United Republic of Tanzania reported only numbers of patients tested and whole percentages of seropositive patients (81).
§Methodology information provided in primary source: “Human sera tested for presence of Zika virus antibody...Only those sera which were found to neutralize 100 or more LD50 have been considered as positive” (52).
¶Methodology information provided in primary source: “Serum was assessed for IgG and IgM antibodies” (83).
## Technical Appendix Table 2. Outbreaks and case reports of laboratory-confirmed Zika virus infection by location, January 1, 1952–February 10, 2016*

<table>
<thead>
<tr>
<th>Continent/country</th>
<th>No. cases</th>
<th>Years</th>
<th>Ref</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Africa</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cape Verde</td>
<td>17</td>
<td>2015</td>
<td>(86)</td>
<td>15 IgM positive only; 2 positive by reverse transcription PCR</td>
</tr>
<tr>
<td>Gabon</td>
<td>5</td>
<td>2007–2010</td>
<td>(23)</td>
<td></td>
</tr>
<tr>
<td>Nigeria</td>
<td>5</td>
<td>1952, 1971–1975</td>
<td>(2,75)</td>
<td></td>
</tr>
<tr>
<td>Uganda</td>
<td>1</td>
<td>Not specified</td>
<td>(40)</td>
<td></td>
</tr>
<tr>
<td><strong>Asia</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cambodia</td>
<td>1</td>
<td>2010</td>
<td>(56)</td>
<td></td>
</tr>
<tr>
<td>Indonesia</td>
<td>7</td>
<td>1977–1978</td>
<td>(24)</td>
<td></td>
</tr>
<tr>
<td>Japan</td>
<td>3</td>
<td>2013–2014</td>
<td>(87,88)</td>
<td>Imported cases (ex-Thailand, ex-French Polynesia)</td>
</tr>
<tr>
<td>Thailand</td>
<td>7</td>
<td>2012–2014</td>
<td>(89)</td>
<td></td>
</tr>
<tr>
<td>Philippines</td>
<td>1</td>
<td>2012</td>
<td>(67)</td>
<td></td>
</tr>
<tr>
<td><strong>Caribbean</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dominican Republic</td>
<td>10</td>
<td>2016</td>
<td>(90)</td>
<td>8 local cases; 2 imported cases (ex-El Salvador)</td>
</tr>
<tr>
<td>Guadeloupe</td>
<td>10</td>
<td>2016</td>
<td>(91)</td>
<td></td>
</tr>
<tr>
<td>Jamaica</td>
<td>1</td>
<td>2016</td>
<td>(92)</td>
<td></td>
</tr>
<tr>
<td>St. Croix, US Virgin Islands</td>
<td>1</td>
<td>2016</td>
<td>(93)</td>
<td></td>
</tr>
<tr>
<td><strong>Central America</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Costa Rica</td>
<td>2</td>
<td>2016</td>
<td>(94)</td>
<td>1 case imported (ex-Colombia); other case not specified</td>
</tr>
<tr>
<td>Mexico</td>
<td>3</td>
<td>2015</td>
<td>(95)</td>
<td>2 local cases; 1 imported case (ex-Colombia)</td>
</tr>
<tr>
<td>Nicaragua</td>
<td>2</td>
<td>2016</td>
<td>(91,96)</td>
<td></td>
</tr>
<tr>
<td><strong>Europe</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Denmark</td>
<td>1</td>
<td>2016</td>
<td>(91,97)</td>
<td>Imported case (ex-Mexico and Brazil)</td>
</tr>
<tr>
<td>Finland</td>
<td>1</td>
<td>2015</td>
<td>(3)</td>
<td>Imported case (ex-Maldives)</td>
</tr>
<tr>
<td>France</td>
<td>1</td>
<td>2013</td>
<td>(98)</td>
<td>Imported case (ex-French Polynesia)</td>
</tr>
<tr>
<td>Germany</td>
<td>4</td>
<td>2013, 2014, 2016</td>
<td>(57,99,100)</td>
<td>Imported cases (ex-Haiti, ex-Malaysian Borneo, ex-Thailand)</td>
</tr>
<tr>
<td>Italy</td>
<td>3</td>
<td>2013–2014, 2015</td>
<td>(60,101)</td>
<td></td>
</tr>
<tr>
<td>Netherlands</td>
<td>13</td>
<td>2015</td>
<td>(102,103)</td>
<td>Imported cases (ex-Suriname [1]; country of import unspecified [12])</td>
</tr>
<tr>
<td>Norway</td>
<td>1</td>
<td>2013</td>
<td>(61)</td>
<td>Imported case (ex-Tahiti)</td>
</tr>
<tr>
<td>Portugal</td>
<td>5</td>
<td>2016</td>
<td>(91,104)</td>
<td>Imported cases (ex-Brazil)</td>
</tr>
<tr>
<td>Spain</td>
<td>7</td>
<td>2016</td>
<td>(105)</td>
<td>Imported cases (country of import unspecified)</td>
</tr>
<tr>
<td>Sweden</td>
<td>1</td>
<td>2015</td>
<td>(91,106)</td>
<td>Imported case (country of import unspecified)</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>6</td>
<td>2014–2016</td>
<td>(107)</td>
<td>Imported cases (ex-Colombia [3], ex-Cook Islands [1], ex-Guyana/Suriname [1], and ex-Mexico/Venezuela [1])</td>
</tr>
<tr>
<td><strong>North America</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Canada</td>
<td>2</td>
<td>2013, 2016</td>
<td>(14,46)</td>
<td>Imported cases (ex-Thailand, ex-El Salvador)</td>
</tr>
<tr>
<td>United States</td>
<td>56</td>
<td>2008, 2013, 2016</td>
<td>(10,12,36,68)</td>
<td>Cases reported in Arkansas (1), California (2), Colorado (3), Delaware (1), District of Columbia (3), Florida (16), Georgia (1), Hawaii (4), Illinois (3), Massachusetts (2), Minnesota (1), Nebraska (2), New Jersey (1), New York (1), Ohio (1), Oregon (1), Pennsylvania (2), Virginia (1), Texas (10). All were imported cases, except for 2 autochthonous sexually-acquired cases, including 1 in Colorado and 1 in Texas. Reported locations of import include Senegal, French Polynesia, South America, Easter Island, and Hawaii.</td>
</tr>
<tr>
<td><strong>Oceania</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Australia</td>
<td>3</td>
<td>2014 (1 case); year unspecified</td>
<td>(39,108,109)</td>
<td>Imported cases (ex-Indonesia [2], ex-Cook Islands [1])</td>
</tr>
<tr>
<td>Cook Islands</td>
<td>50</td>
<td>2014</td>
<td>(6)</td>
<td>932 additional suspected cases</td>
</tr>
<tr>
<td>Easter Island</td>
<td>53</td>
<td>2014</td>
<td>(7,110,111)</td>
<td>One imported case (ex-Tahiti); 40 additional suspected cases</td>
</tr>
</tbody>
</table>
References: ([72x110]burning sensation of throat, cough, stomach pain, anorexia, lightheadedness, dizziness, chills, oral aphthous ulcers, photophobia, lymphadenopathy, hematospermia, hematuria, hypotension, gingival bleeding, hearing loss, pruritus, malaise, diarrhea, nausea/vomiting, constipation, edema, sore throat, cough, stomach pain, anorexia, lightheadedness, dizziness, chills, oral aphthous ulcers, photophobia, lymphadenopathy, rhinorrhea, and burning sensation of palms/soles.

Technical Appendix Table 3. Symptoms and sequelae of 195 symptomatic patients with confirmed Zika virus infection reported in Peer-reviewed literature for 1964–2016*

<table>
<thead>
<tr>
<th>Symptom</th>
<th>No. of patients</th>
<th>% Total patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rash</td>
<td>131</td>
<td>67.2</td>
</tr>
<tr>
<td>Fever</td>
<td>124</td>
<td>63.6</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>56</td>
<td>28.7</td>
</tr>
<tr>
<td>Myalgia</td>
<td>46</td>
<td>23.6</td>
</tr>
<tr>
<td>Headache</td>
<td>42</td>
<td>21.5</td>
</tr>
<tr>
<td>Conjunctivitis</td>
<td>40</td>
<td>20.5</td>
</tr>
<tr>
<td>Retroorbital pain</td>
<td>22</td>
<td>11.3</td>
</tr>
<tr>
<td>Edema</td>
<td>19</td>
<td>9.7</td>
</tr>
<tr>
<td>Pruritus</td>
<td>15</td>
<td>7.7</td>
</tr>
<tr>
<td>Fatigue/asthenia</td>
<td>14</td>
<td>7.2</td>
</tr>
</tbody>
</table>

*Data represent reports that included clinical symptoms and sequelae for all symptomatic patients with laboratory-confirmed Zika virus infection (confirmed by serology and/or RT-PCR, or mode of laboratory testing not specified), with a complete and detailed account of symptoms reported in peer-reviewed literature for January 1, 1964–February 3, 2016 (age range of patients was 4 days–76 years). Reports only for this period included symptoms and therefore met criteria for inclusion in the table. Patients may have experienced >1 symptom. Less prevalent reported symptoms and sequelae (>5% of patients with reported symptoms) include microcephaly, cerebral calcifications, Guillain-Barré syndrome, prostatitis, hematospermia, hematuria, hypotension, gingival bleeding, hearing loss, pruritus, malaise, diarrhea, nausea/vomiting, constipation, edema, sore throat, cough, stomach pain, anorexia, lightheadedness, dizziness, chills, oral aphthous ulcers, photophobia, lymphadenopathy, rhinorrhea, and burning sensation of palms/soles.

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