Incidence Rate for Hantavirus Infections without Pulmonary Syndrome, Panama

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During 2001–2007, to determine incidence of all hantavirus infections, including those without pulmonary syndrome, in western Panama, we conducted 11 communitywide surveys. Among 1,129 persons, antibody prevalence was 16.5%–60.4%. Repeat surveys of 476 found that patients who seroconverted outnumbered patients with hantavirus pulmonary syndrome by 14 to 1.

In the Americas, hantavirus species that occur at low frequency are associated with the severe disease hantavirus pulmonary syndrome (HPS) (1,2), and species that occur at higher frequency are associated with milder disease (3–5). In Panama, HPS is caused by the Choclo virus, for which a common rodent, the fulvous pygmy rice rat (6), is host. Serum antibody prevalence against this virus is 3%–33% in neighborhoods where HPS cases have occurred (7) and 16%–45% according to selected communitywide surveys (8). Neutralization-inhibition assays of antibody-positive serum indicated past infections caused by Choclo virus (9). To obtain a more accurate incidence of hantavirus infections in Panama, we conducted repeat surveys to identify hantavirus seroconversions during 1- to 3-year intervals between surveys. Our goal was to compare incidence of seroconversion with that of concurrent HPS in the same communities.

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The Study

During 2001–2007, a total of 4 communities (3 in Los Santos Province and 1 in Veraguas Province) within hantavirus-endemic agroecosystems in western Panama were sampled 2–4 times at 1- to 3-year intervals (Table 1). Informed written consent was obtained from all adult participants and from parents or legal guardians of minors. Consent and assent forms were reviewed and approved by institutional ethics review boards at the University of New Mexico, the Gorgas Memorial Institute in Panama City, and the protocol review committee of the International Centers for Infectious Diseases Research program of the National Institute of Allergy and Infectious Diseases. Eligible participants were all adults and children >2 years of age who permanently resided in each community according to the 2000 national census. The reasons for noninclusion in the first and subsequent surveys were absence during the week of the survey and refusal to participate.

A questionnaire administered to the head of household asked for a history of respiratory-related illnesses and hospitalizations within the past 3 years. Venous blood was collected from all family members for serologic testing. Results of the surveys were provided to each participating community through community meetings. Surveillance for HPS was conducted in the same communities as the serosurvey and nationally through reports to the Ministry of Health, and cases of HPS were confirmed by questionnaire. The diagnosis of HPS required finding immunoglobulin (Ig) M in acute-phase serum, detection of Choclo virus RNA in serum by reverse transcription PCR, typical respiratory signs and symptoms, and chest radiographic findings compatible with pulmonary edema.

Heparinized whole blood collected by arm venipuncture was separated by centrifugation; plasma was stored at −20°C until analysis. In binding assays, antibody to all known hantaviruses indigenous to the Americas cross-react with the N protein of Sin Nombre virus (10). A strip immunoblot assay for IgG containing recombinant N protein of the 3H226 genotype of Sin Nombre virus was used as described (10); the criterion for positivity was a dark band for Sin Nombre N protein at a serum dilution of 1:200. An enzyme immunoassay used recombinant nucleocapsid protein from Sin Nombre virus (11); the cutoff value was established at 3 SD above reactivity to a panel of known positive serum. All samples were tested by both assays; the concordance of the enzyme immunoassay and strip immunoblot assay in this study was 97%, and the criterion for seropositivity was a positive reaction in both assays. Loss of antibody in persons with previously positive serum was determined by 2 independent tests with both assays. IgM against hantavirus was not tested. In Panama, all HPS patients tested have had positive reverse transcription PCR results.
for Choclo genomic RNA in acute-phase blood samples (9), and antibody has been detected by both assays.

Data were transferred from field collection forms to a database (Epi Info version 6.04d, Centers for Disease Control and Prevention, Atlanta, GA, USA) for statistical analyses using Epi Info software. Changes in seroprevalence within each community were tested by Fisher exact test for each interval and by longitudinal analysis for all intervals and communities by a generalized estimating equation (12). Increases in seroprevalence according to community and year of survey were tested by analysis of covariance.

The 11 surveys repeatedly sampled 60%–85% of the total population of each community, for a total of 1,838 samples from 1,129 persons. Overall antibody prevalence was 32.9%, varying from 16.5% to 60.4% in individual surveys (Table 1). In each of the 3 Los Santos communities (Agua Buena, Isla Cañas, San Jose), seroprevalence increased annually by ≈5% (Table 1); the overall seroprevalence increases for the combined Los Santos localities and year, p = 0.0014.

Table 1. Hantavirus seroprevalence, western Panama*

<table>
<thead>
<tr>
<th>Community and year of survey</th>
<th>Community population</th>
<th>Persons tested, no. (%) of community</th>
<th>No. (%) IgG positive†</th>
<th>No. undergoing follow-up testing‡</th>
<th>Repeated tests only: no. (%) IgG positive†§</th>
</tr>
</thead>
<tbody>
<tr>
<td>Agua Buena</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2003</td>
<td>175</td>
<td>105 (60)</td>
<td>47 (44.8)</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>2004</td>
<td>175</td>
<td>108 (62)</td>
<td>59 (54.6)</td>
<td>75</td>
<td>41 (54.7)</td>
</tr>
<tr>
<td>2006</td>
<td>160</td>
<td>102 (64)</td>
<td>61 (60.4)</td>
<td>69</td>
<td>42 (61.8)</td>
</tr>
<tr>
<td>2007</td>
<td>164</td>
<td>99 (60)</td>
<td>49 (49.5)</td>
<td>55</td>
<td>33 (60.0)</td>
</tr>
<tr>
<td>Isla Cañas</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2001</td>
<td>276</td>
<td>223 (81)</td>
<td>74 (33.2)</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>2003</td>
<td>184</td>
<td>120 (65)</td>
<td>56 (46.7)</td>
<td>90</td>
<td>44 (48.9)**</td>
</tr>
<tr>
<td>2006</td>
<td>187</td>
<td>120 (64)</td>
<td>63 (52.5)</td>
<td>49</td>
<td>26 (53.1)#</td>
</tr>
<tr>
<td>San Jose</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2001</td>
<td>593</td>
<td>486 (82)</td>
<td>80 (16.5)</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>2003</td>
<td>454</td>
<td>327 (72)</td>
<td>84 (25.7)</td>
<td>270</td>
<td>70 (25.7)#</td>
</tr>
<tr>
<td>2006</td>
<td>85</td>
<td>61 (72)</td>
<td>19 (31.1)</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>2006</td>
<td>93</td>
<td>87 (94)</td>
<td>23 (26.4)</td>
<td>41</td>
<td>11 (26.8)</td>
</tr>
</tbody>
</table>

Table 2. Hantavirus seroconversions and HPS cases, western Panama*

<table>
<thead>
<tr>
<th>Community and survey intervals</th>
<th>No. undergoing follow-up testing†</th>
<th>No. seroconverted/ no. seronegative‡</th>
<th>No. conversions/100 person-years</th>
<th>No. seroreverted/ no. seropositive§</th>
<th>No. HPS cases¶</th>
</tr>
</thead>
<tbody>
<tr>
<td>Agua Buena</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1</td>
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<tr>
<td>2003–2004</td>
<td>75</td>
<td>8/42</td>
<td>0/33</td>
<td>4/40</td>
<td>0</td>
</tr>
<tr>
<td>2004–2006</td>
<td>69</td>
<td>6/29</td>
<td>4/10</td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>2006–2007</td>
<td>55</td>
<td>5/23</td>
<td>1/3</td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>19</td>
<td>15.4</td>
<td>11</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Isla Cañas</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>2001–2003</td>
<td>90</td>
<td>18/64</td>
<td>0/26</td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>2003–2006</td>
<td>49</td>
<td>2/24</td>
<td>1/25</td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>20</td>
<td>10.0</td>
<td>1</td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>San Jose</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>3</td>
</tr>
<tr>
<td>2001–2003</td>
<td>270</td>
<td>29/228</td>
<td>1/42</td>
<td></td>
<td>3</td>
</tr>
<tr>
<td>Total</td>
<td>29</td>
<td>6.4</td>
<td>1</td>
<td></td>
<td>3</td>
</tr>
<tr>
<td>Borracherones</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>2003–2006</td>
<td>41</td>
<td>2/26</td>
<td>6/15</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>2</td>
<td>2.6</td>
<td>6</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Study totals</td>
<td>70</td>
<td>8.2</td>
<td>16</td>
<td></td>
<td>5</td>
</tr>
</tbody>
</table>

*HPS, hantavirus pulmonary syndrome.
† No. persons repeat tested in this and previous survey.
‡ No. seroconverted among subset who were seronegative at the beginning of the interval.
§ No. seroreverted among subset who were seropositive at the beginning of the interval.
¶ HPS cases verified by Ministry of Health during interval in community.
Conclusions

Antibody prevalence surveys are useful for identifying populations and locations at risk, monitoring changes in incidence, and focusing limited public health resources. Determining whether the observed increases in seroprevalence will be sustained requires additional surveys, but this information will be useful as the new agroeconomy increasingly emphasizes the monoculture of products (rice and sugar cane) favorable to rodents (14). Nonetheless, the documentation of large numbers of mild or asymptomatic hantavirus infections not progressing to HPS has identified a larger effect of this zoonotic disease.

Acknowledgments

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