PREVALENCE OF ANTIBODIES TO HANTAVIRUS AMONG FAMILY AND HEALTH CARE WORKER CONTACTS OF PERSONS WITH HANTAVIRUS CARDIOPULMONARY SYNDROME: LACK OF EVIDENCE FOR NOSOCOMIAL TRANSMISSION OF ANDES VIRUS TO HEALTH CARE WORKERS IN CHILE

CONSTANZA CASTILLO, ELIECER VILLAGRA, LIGIA SANHUEZA, MARCELA FERRES, JOVITA MARDONES, AND GREGORY J. MERTZ

INTRODUCTION

Hantaviruses are transmitted from rodents to humans, and person-to-person transmission has not been proven with hantavirus infection in humans in Asia, Europe, or North America. Family clusters of hantavirus cardiopulmonary syndrome (HCPS) have been observed in Argentina and Chile. In Chile, approximately 30% of HCPS cases reported occurred in family clusters. In most cases, the family members shared a common exposure to a rodent-contaminated environment. However, in some clusters only the index case had exposure to rodents in a rural area, and the additional cases, such as close household contacts that live in low-risk urban settings, had no apparent exposure to hantavirus other than exposure to the index case.

To make a preliminary assessment of the risk of person-to-person transmission of Andes virus, we conducted a cross-sectional seroprevalence and epidemiologic study among contacts of index cases in region IX of Chile, where one-third of the Chilean hantavirus cases have occurred. Region IX is located in southern Chile between latitudes 37° and 40°S and longitudes 70° and 74°E.

MATERIAL AND METHODS

We studied 215 contacts of 20 HCPS cases admitted to the Temuco Teaching Hospital in Temuco, Chile. All index cases shared a risk activity for exposure to hantavirus such as cleaning storage buildings or closed facilities, working in the forest, or sleeping in inhabited cottages. The diagnosis of HCPS was done using clinical and laboratory criteria developed by the United States Centers for Disease Control and Prevention (CDC). The contacts were identified using the database of the Epidemiology Division of Chilean Ministry of Health, which allowed us to identify all probable contacts of the 20 index cases diagnosed between 1998 and the first months of 2000. Direct contact was defined as anyone who shared housing or lodging for one or more days or stayed in closed facilities for longer than one hour with an HCPS patient during the prodromal or cardiovascular stage of the disease.

Direct contact for a health care worker was defined as caring directly for a patient, performing intubation, suctioning of respiratory secretions, cardiopulmonary resuscitation, and venous or arterial punctures, handling body fluids (blood, urine, respiratory secretions), or performing an autopsy. We assumed that family or health care worker contacts were exposed to respiratory aerosols if they came within two meters of the patient. Every subject who met the entry criteria of direct contact with an HCPS patient was included after signing an informed consent form that was reviewed and approved by the Ethics Committee of Temuco Teaching Hospital. This committee also reviewed and approved the study protocol. A questionnaire for collecting epidemiologic information was completed and a blood sample for detection of specific antibodies to hantavirus was obtained.

Laboratory techniques. Detection of specific IgG antibodies against hantavirus was done using an enzyme immunoabsorbent assay (EIA) following the CDC guidelines using antigens of Sin Nombre virus provided by the CDC. Titers > 1:400 and an optical density (OD) > 2.0 were considered positive. The EIA was repeated with Andes virus antigen provided by the Malbrán Institute (Buenos Aires, Argentina). The assays were performed at the Public Health Institute in Santiago, Chile. All indeterminate and positive samples were retested using a strip immunoblot assay (SIA) with Sin Nombre virus antigens at the Infectious Disease and Virology Laboratory at the Catholic University of Chile (Santiago, Chile) by staff members who were blind to the epidemiologic information.

Statistical analysis. The chi-square test or Fisher’s exact test was used to compare proportions between family members and health care workers. The prevalence of antibodies to hantavirus was calculated for family members and health care workers based on the proportion of contacts positive for antibodies to hantavirus. The 95% exact binomial confidence intervals (CIs) on the prevalence estimates were based on the method of Blyth-Still-Casella.

RESULTS

We identified 120 family contacts and 125 health care workers. Among the 120 family contacts identified, 106 met the entry criteria. The mean age of the family members was 31.0
years, 65.7% were males, and 76.2% lived in rural areas (Table 1).

The main activities common with the index case were sharing housing (45.7%) or lodging (44.8%). One-third of the subjects (34.3%) were not related but worked with the patient in a closed room or shared transportation for more than one hour (31.1%). All family contacts were exposed to respiratory aerosols of the index case (Table 2).

Potential environmental exposure to hantavirus was present in most of the family contacts’ homes, such as storage of firewood (76.2%), presence of bushes next to the home (74.3%), and storage of garbage (44.8%). Agricultural activities included cleaning of barns (63.5%), storing products (44.7%), and cutting bushes (39.1%). Rodents or rodents’ feces were observed around the houses in 88.6%, in the work places in 72.4% and inside their homes in 59.1% (Table 3).

Among 125 health care workers that were screened, 109 were enrolled. The mean age of the healthcare workers was 39.3 years, and most (67.9%) were female. All but one of the health care workers lived in urban areas (Table 1).

Health care workers were exposed to respiratory aerosols (99.1%), blood (56.0%), tracheal secretions (45.9%), and other body fluids (12.8%) (Table 2). Universal precautions were followed, and surgical masks were used when inserting or suctioning endotracheal tubes. No protective eyewear was available. The nursing assistants wore gloves, and 30% used gloves and masks for general care of the patient. The autopsy assistant wore a laboratory coat, surgical mask, and gloves. The majority of staff cared for patients during the cardiopulmonary stage of the disease. Only 10 (9.17%) had direct contact during the prodromal stage.

The prevalence of antibodies against hantavirus was 1.9% (95% CI = 0.34–6.3%) in family member contacts compared with 0.0% (95% CI = 0–3.2%) in the health care workers. In the two seropositive family contacts, the EIA titers were: 1:1,600 (OD = 3.39) and 1:6,400 (OD = 7.84), respectively, and these two samples were also positive by the SIA.

**DISCUSSION**

The seroprevalence among the family members was 1.9%, which is similar to the seroprevalence of 2.5–7.5% in the rural communities where they live. In the present study, no antibodies to Andes virus were found in health care workers. In studies in persons with Sin Nombre virus-associated HCPS

<table>
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<tr>
<th>Table 1</th>
<th>General characteristics of contacts with cases of hantavirus cardiopulmonary syndrome (HCPS) in region IX of Chile</th>
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<tbody>
<tr>
<td>Contacts</td>
<td>Family members (n = 106)</td>
</tr>
<tr>
<td>Male, %</td>
<td>65.7</td>
</tr>
<tr>
<td>Female, %</td>
<td>34.3</td>
</tr>
<tr>
<td>Residence</td>
<td></td>
</tr>
<tr>
<td>Urban</td>
<td>24</td>
</tr>
<tr>
<td>Rural</td>
<td>76</td>
</tr>
<tr>
<td>Residence†</td>
<td></td>
</tr>
<tr>
<td>High risk</td>
<td>95.2</td>
</tr>
<tr>
<td>Low risk</td>
<td>4.8</td>
</tr>
</tbody>
</table>

* By chi-square test.
† Communities where HCPS patients acquired the clinical disease were considered high-risk areas.

<table>
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<tr>
<th>Table 2</th>
<th>Exposure to respiratory aerosols and/or body fluids of patients with hantavirus cardiopulmonary syndrome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exposure to body fluids*</td>
<td>Family members (n = 100)</td>
</tr>
<tr>
<td>Respiratory aerosols</td>
<td>100</td>
</tr>
<tr>
<td>Blood</td>
<td>0</td>
</tr>
<tr>
<td>Tracheo-bronchial secretions</td>
<td>0</td>
</tr>
</tbody>
</table>

* Exposure to more than one kind of body fluid occurred.
† By Fisher’s exact test.

in the southwestern United States, measurements by a quantitative polymerase chain reaction suggests that the viremia is higher during the prodromal stage and decreases rapidly during the cardiovascular stage of the disease. In addition, Andes virus was isolated from the serum of a 10-year-old Chilean boy two days prior to the onset of symptoms and before development of antibodies. These scanty data suggest that viremia decreases rapidly after the onset of clinical disease and that contagiousness may be greater during the prodromal phase than during the cardiopulmonary phase. The finding that most of the health care workers had contact with the index cases beginning with the cardiopulmonary stage may explain in part, but not prove, why there are no cases among health care workers in Chile and why the few cases of apparent person-to-person transmission in Chile have been in family contacts who have been with the index case early in the course of illness.

Person-to-person transmission of Andes virus was reported in an outbreak of HCPS in El Bolsón and Bariloche in southern Argentina in 1996.5 This epidemic cluster predominantly affected family members of index cases and health care workers who also were family members or were socially related to the patients. However, a physician residing in Buenos Aires who did not visit the endemic areas of southern Argentina developed HCPS after direct contact with a patient with HCPS in Buenos Aires.4 Furthermore, genetic analysis showed that a single virus caused the outbreak.5 There is no information about the type of infection control measures that were used during the outbreak in Argentina, and as such, there is no way to determine whether differences in infection control practices could explain the lack of nosocomial transmission in our study. A North American serosurvey study that included 266 health care workers who had direct contact with HCPS cases due to Sin Nombre Virus found that none had antibodies against hantavirus.15 In our study, there was no evidence of nosocomial transmission and no clear evidence of person-to-person transmission among the family contacts. In most cases, family members shared the same risk factors
for HCPS, including exposure to a common environmental source of infection. The two seropositive family contacts worked inside the same storage buildings where the two index patients acquired HCPS.

In conclusion, the seroprevalence in family and health care worker contacts of persons with HCPS was similar to the seroprevalence in the surrounding community. Our data suggest that there is no evidence for nosocomial transmission of Andes virus in region IX of Chile.

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REFERENCES