Original Contribution

Temporal and Spatial Host Abundance and Prevalence of Andes Hantavirus in Southern Argentina

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Abstract: Andes virus (AND) is a hantavirus hosted by the sigmodontine rodent *Oligoryzomys longicaudatus* in southern Argentina, where it is responsible for most cases of hantavirus pulmonary syndrome (HPS). Our study provides data about the spatial variation in abundance of the rodent host of AND hantavirus. We report results of a longitudinal study performed in a locality of the Andean region of Chubut Province. From November 2003 (spring) to July 2006 (winter), *O. longicaudatus* was the most common species captured (63%) and it showed significant differences in abundance among habitats and seasons. Most antibody-positive rodents were *O. longicaudatus* (9.2%), followed by *A. longipilis* (3.6%) and *A. olivaceus* (1.5%). The highest number of antibody-positive animals was observed for males that belonged to the heaviest mass classes. Antibody-positive *O. longicaudatus* were more abundant in brush habitats. We found low richness of rodents and abundance of *O. longicaudatus* in areas affected by anthropogenic activity. The infection seems to be regionally persistent, but the risk to humans in a landscape would be localized. To develop accurate models for predicting HPS outbreaks, further research is needed to characterize rodent movement patterns across the landscape.

Keywords: *Oligoryzomys longicaudatus*, abundance fluctuations, hantavirus pulmonary syndrome

INTRODUCTION

Hantavirus pulmonary syndrome (HPS) is a human disease caused by some members of the genus Hantavirus, family Bunyaviridae. Some hantaviruses are known to be highly pathogenic for humans (e.g., Sin Nombre virus (SNV), Bayou virus, Black Creed Canal virus, New York virus (Nichol et al., 1993; Childs et al., 1994; Khan et al., 1995;

Morzunov et al., 1995; Rollin et al., 1995). Each distinct form of the virus is closely associated with a single, or possibly a few, rodent species belonging to Murinae, Arvicolinae, and Sigmodontinae subfamilies within the Rodentia Order (Schmaljhon and Hjelle, 1997; Enría and Levis, 2004). The virus is maintained in nature by transmission among rodent populations, which may occur through fighting and social grooming (Young et al., 1998), and it is transmitted to humans through aerosolized particles from contaminated excreta of rodents (Glass, 1997; Mills, 1999; Douglas et al., 2001; Padula et al., 2004).

Hantaviruses have been recorded in four regions in Argentina. These viruses are associated with several species of indigenous sigmodontine rodents that are typical of the different regions (Riera et al., 1994; Padula et al., 2000). These regions differ in their landscape types, vegetation types, primary agricultural production, and agricultural practices (Cabrera, 1976). Nine hantavirus genotypes have been recorded in those four regions: Orán (ORN), Bermejo (BMJ) and Laguna Negra viruses in the northwest (Salta and Jujuy provinces), Pergamino (PER), Maciel (MAC), Lechiguanas (LEC), and Hu 39694 viruses in the central region (Buenos Aires, Entre Ríos and Santa Fe provinces), Juquitiba in the northeast (Misiones and Formosa provinces), and Andes (AND) virus in the south of the country (Chubut, Neuquén and Río Negro provinces) (Enría and Pinheiro, 2000; Levis et al., 1998, 2004). All genotypes, except for Maciel and Pergamino virus, have been associated with human disease (Levis et al., 1998). Hantavirus pulmonary syndrome cases are unevenly distributed in space and time in the four regions (Levis et al., 1995, 1998, 2004; López et al., 1996; Calderón et al., 1999; Padula et al., 2000; Martínez et al., 2001; González Della Valle et al., 2002; Sosa Estaini et al., 2002; Mills et al., 2007).

Andes hantavirus has been responsible for the HPS cases recorded in the south of Argentina and Chile since 1995 (López et al., 1996; Padula et al., 2000). Previous studies have revealed that in these areas, *O. longicaudatus* is the most common and widespread rodent species (Pearson and Pearson, 1982; Pearson, 1983, 2002; Murúa and González, 1986; Meserve and Le Boulengé, 1987; Meserve et al., 1996; Piudo et al., 2005) and shows a high prevalence (up to 18%) of AND virus-reactive antibody (Calderón et al., 1999; Cantoni et al., 2001; Larrieu et al., 2003; Padula et al., 2004; Piudo et al., 2005). *Oligoryzomys longicaudatus* occurs in multiple habitat types over a large geographic range (Porcasi et al., 2005). This rodent species has been captured in disturbed habitats (cultivated field borders and peridomestic settings), as well as in primary pastures, brushes, and forest areas in Argentina (Pearson, 1983, 2002; Monjeau et al., 1998; Pardiñas et al., 2000, 2003; Piudo et al., 2005). Host population and pathogen prevalence may vary on local scales (Mills, 1999) and studies on *O. longicaudatus* habitat use in Chile indicate a substantial difference among habitat types (Murúa and González, 1982; González et al., 2000).

Many rodent species demonstrate distinct local habitat preferences, so the risk of human disease may be more precisely defined by describing differences in host distribution, population densities, and prevalence of infection among the distinct habitats represented in a local area (Mills, 1999). Moreover, the rodent assemblage structure and prevalence of AND may be influenced by seasonal variables. In Chile rodent populations may show from 5- to 10-fold changes in density between autumn (high-density season) and early spring (low-density season), but in Argentina changes in the annual population density and more precisely, changes in the infected animals density are scarcely known (Cantoni et al., 2001; Pearson, 2002). Accordingly, we ask: Is prevalence of infection in host population related to host abundance, individuals' sex and/ or age, habitat and/or assemblage structure? We examined spatial heterogeneity and seasonal variation in rodent populations and AND prevalence among them in the southern region of Argentina.

METHODS

Study Area

The study was performed from November (spring) 2003 to July (winter) 2006 in Cholila (42°31′ S; 71°27′ W), Andean region, Chubut Province (Fig. 1). The study area is a steppe-rainforest transition zone. The topography is primarily mountainous with most features formed by glacial processes (Cabrera and Willink, 1980). The dominant climate is temperate with most rainfall occurring between April and September (600 mm). There is an abrupt precipitation gradient from west to east due to the rain shadow effect of the Andes, which results in a strongly defined vegetation structure and floristic composition (Cabrera and Willink, 1980; León et al., 1998). Phytogeographically, this region corresponds to "Dominio Subantártico," "Distrito del bosque Caducifolio," characterized by two deciduous *Nothofagus* species: *N. antartica* (ñire) and *N. pumilio* (lenga), and *Austrocedrus chilensis* (ciprés de la cordillera) in the septentrional zone (Cabrera and Willink, 1980).

Our study region (420 km²) in Cholila included four valleys: El Cajón, El Rincón, El Blanco, and Villa Lago Rivadavia with approximately 2,000 inhabitants. Rodent populations were sampled in four types of habitats, selected as the most representative in the landscape: brushes, pastures, forests, and peridomestic areas. Brushes were characterized by native species, such as calafate, romerillo, espino negro, and laura, and nonnative species, such as rosa mosqueta. Forests were dominated by ñire, cohiue, ciprés
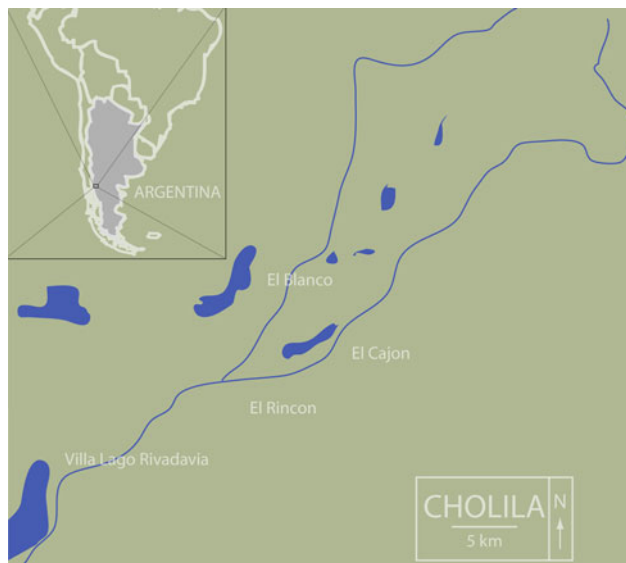
Figure 1. Map of Argentina showing the study area location.

de la cordillera, and lenga (after 1,200 m of height), with or without caña coligüe in the understory. Pastures were defined as habitats where the vegetation coverage did not exceed 50 cm in height and were dominated by gramineous plants. Peridomestic areas included environments with some human use around human houses.

Rodent trapping and processing

Snap traps of two sizes (18 × 7 × 1 cm and 10 × 5 × 1 cm), and live capture traps (Sherman type trap, 23 × 8 × 9.5 cm) were placed in lines and trapped rodents were removed. Twenty-four lines were placed in forest, pasture, and peridomestic habitats, and 15 in the brush habitat, because in this habitat type the estimated abundances values, as relative density index (RDI), were more homogeneous than in the other habitat types. The minimum distance between trapping lines was 200 m. In each habitat type, trapping was undertaken for three consecutive nights, during each season (spring, summer, autumn, and winter). Rodent populations were sampled in four types of habitat in each of the four valleys, where 3–6 lines per habitat type were placed. In brush habitat each line had 20 live traps and 20 snap traps, whereas in the other types of habitat 10 live traps and 10 snap traps were used for each line. Traps were placed at 5-m intervals, alternating one live trap with one snap trap. Traps were baited with a mixture of peanut butter and cow fat.

During trapping periods, traps were checked each morning. Species, sex, and body measurements (weight, lengths of body and tail) were recorded. Male and female reproductive status also was recorded. Rodents captured using live traps were anesthetized with methoxyflurane gas, and blood samples for seroprevalence determination were obtained from the retroorbital sinus. The anesthetized animals were euthanized by overdose of anesthesia before necropsy. The identification of animals was verified by external body features and craniometrical characters and by microsatellites markers in the case of *O. longicaudatus* (González-Ittig et al., 2008). A few voucher specimens of all species were deposited in the Mammals Collection of the Centro Nacional Patagónico (Puerto Madryn, Chubut, Argentina). Handling of rodents followed standardized safety guidelines recommended by the Centre for Disease Control and Prevention (Mills et al., 1995).

Serology

Rodent blood samples were placed in cryovials, centrifuged in the field, and stored in liquid nitrogen until further testing at the Instituto Nacional de Enfermedades Virales Humanas Dr. Julio Maiztegui (INEVH). Hantavirus IgG antibodies were detected by an ELISA test using recombinant SNV nucleocapsid antigen (kindly provided by TG Ksiazed, Childs et al., 1994). Briefly, 96-well polyvinyl microplates were coated with SNV recombinant and control antigen overnight; then, serum samples and positive and negative controls were applied, followed by a mix of peroxidase-conjugated anti-*Rattus norvegicus* and anti-*Peromyscus maniculatus* IgG. The substrate applied was 2,2′-azino-di (3-etilbentiazolin sulfonate) (ABTS, Kierkegaard & Perry Laboratories, Inc., Gaithersburg, MD). Absorbance was measured at 405 and 450 nm. Serum dilutions were considered positive if the optical density was >0.2 after adjusting by subtraction of the corresponding negative-antigen optical density. Serum samples with titers >1:400 were considered positive.

Data analysis

A RDI was used to estimate population abundance in each habitat.

$$\text{RDI} = \frac{\text{number of captures.}}{(\text{number of traps} \times \text{number of nights}) - a} \times 100,$$

where a is the number of shut traps without animals (Castillo et al., 2003). We assumed that a relative measure represents population peaks and troughs, and provides

good estimates of the relative population changes (Debrot, 1981; Saucy, 1994), allowing us to show seasonal and annual abundance fluctuations.

Oligoryzomys longicaudatus–habitat associations were evaluated, as suggested by Mills et al. (1991), by deriving an expected number of captures for the species in each habitat by multiplying the total number of individuals captured by the proportion of trap nights occupied by each habitat type. This expected value was compared to the observed number of captures in a particular habitat and χ^2 values derived. Deviations of observed values from expected values were standardized as percentages of expected values. Significant deviations from expected associations were tested by the use of 95% Bonferroni confidence intervals (Byers et al., 1984; Mills et al., 1991). The assumption in this analysis is that the four different habitat types have the same probability of capture. On the other hand, the number of infected animals and the total number of hosts were estimated by habitat. To determine the expected values, the total number of analyzed animals and the number of seropositive and seronegative analyzed animals were registered by habitat. The relation between the analyzed animals of each habitat and the total area was registered. This relation was multiplied by positive animals of each habitat. Finally, this expected value was compared with the total number of positives of each habitat using χ^2. To know which type of habitat showed higher frequencies of seropositive animals, the percentage of positive animals in relation to the total number of positive animals was calculated.

RESULTS

From November 2003 (spring) to July 2006 (winter), 2,445 rodents were captured during 79,680 trap nights, and 1,331 blood samples were collected. O. longicaudatus was the most common species captured (62.72%), followed by Abrothrix longipilis (14.20%) and A. olivaceus (13.7%). Other less common rodents captured were Loxodontomys micropus (2.55%), Reithrodon auritus (1.03%), Geoxus valdivianus (0.16%), Irenomys tarsalis (0.25%), Akodon iniscatus (0.33%), Chelemys sp (0.45%), and Akodon sp (1.03). The murid Mus musculus also was captured (3.58%).

After adjusting for the number of traps among habitat types, the trap success for O. longicaudatus differed among habitat types (χ^2 = 4648.93; degrees of freedom (df) = 3; $p < 0.001$). The trap success for O. longicaudatus was greater in relatively undisturbed environments (brush,

69.1%; forests, 66.2%) and lower in anthropogenically modified environments (peridomestic settings, 39.7%; pasture, 34%).

A seasonal variation in RDI of O. longicaudatus was observed in brush and forest habitats, with a minimum in spring and a peak in autumn-winter. In brush habitats the peak was in winter, whereas in forests it was registered in summer and autumn. O. longicaudatus were scarce in peridomestic and pasture habitats (Fig. 2).

Individuals of O. longicaudatus, A. olivaceus, and A. longipilis had reactive antibodies to hantavirus (Table 1). Most antibody-positive rodents were O. longicaudatus (9.2%), followed by A. longipilis (3.6%) and A. olivaceus (1.5%). Antibody-positive animals belonging to A. olivaceus and A. longipilis species were trapped when the abundance of O. longicaudatus was low. The hantavirus prevalence in O. longicaudatus was greater in spring and winter throughout the 4 years sampled.

Antibody-positive O. longicaudatus were captured in all habitats (Fig. 3). The number of antibody-positive individuals showed a significant degree of heterogeneity between habitat types (χ^2 = 222.1647; df = 3; $p < 0.001$), with the greatest values in brush habitats. In forests the greatest number of positive animals coincided with the greatest abundance period (summer-autumn); meanwhile in brush habitats the infection peak was in winter and spring (Fig. 3). The greatest number of positive lines (where antibody-positive O. longicaudatus was captured) was recorded in brush habitats throughout the whole sampling period (Table 2).
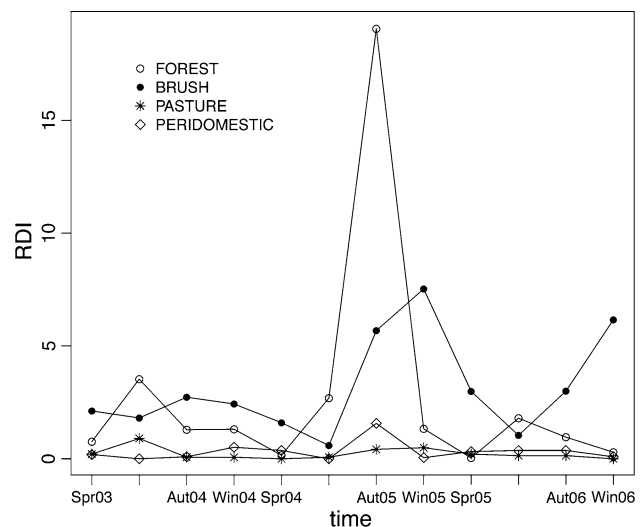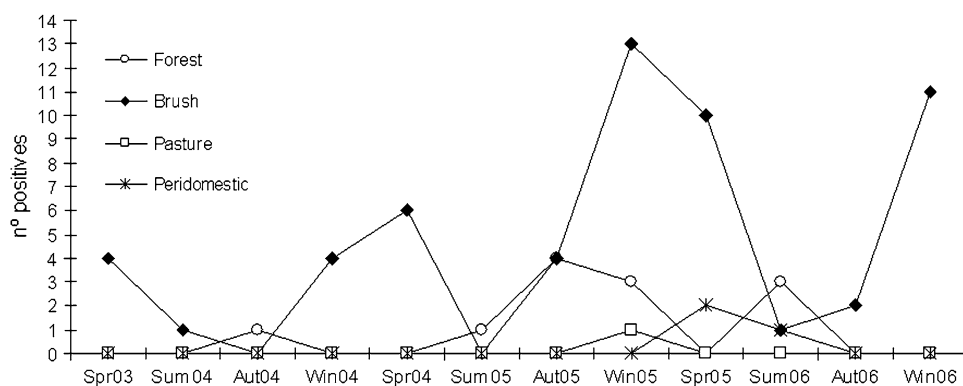

Figure 2. Seasonal relative abundance (RDI) of O. longicaudatus by habitats in Cholila (Chubut) in spring (Spr), summer (Sum), autumn (Aut), and winter (Win) of 2003–2006.

Table 1. Hantavirus antibody prevalence in blood samples of wild rodents in Cholila (Chubut, Argentina) (Spring 2003–Winter 2006)

	Total sp Pos/test (prev)	*O. longicaudatus* Pos/test (prev)	*A. olivaceus* Pos/test (prev)	*A. longipilis* Pos/test (prev)
Spr03	5/22 (22.7)	4/9 (44.4)	1/5 (16.7)	0/7 (0)
Sum04	2/48 (4.2)	1/25 (4)	0/14 (0)	1/9 (11.1)
Aut04	1/22 (4.5)	1/13 (7.7)	0/5 (0)	0/4 (0)
Win04	5/72 (6.9)	4/50 (8)	1/12 (8.3)	0/10 (0)
Spr04	7/84 (8.33)	6/45 (13.3)	0/7 (0)	1/32 (3.1)
Sum05	2/60 (3.3)	1/40 (2.5)	0/6 (0)	1/14 (7.1)
Aut05	9/414 (2.2)	8/325 (2.5)	0/52 (0)	1/37 (2.7)
Win05	17/190 (8.9)	17/169 (10.1)	0/8 (0)	0/13 (0)
Spr05	13/87 (14.9)	12/59 (20.4)	0/15 (0)	1/13 (7.7)
Sum06	6/80 (7.5)	5/45 (11.1)	0/14 (0)	1/21 (4.8)
Aut06	3/113 (2.6)	2/80 (2.5)	0/19 (0)	1/14 (7.1)
Win06	11/139 (7.9)	11/118 (9.3)	0/10 (0)	0/11 (0)

Figure 3. Seasonal number of positive individuals of *O. longicaudatus* by habitat (Cholila, Chubut) in spring (Spr), summer (Sum), autumn (Aut), and winter (Win) of 2003–2006.

Males had anti-hantavirus antibodies more frequently than females (11.18% of 626 individual males vs. 3.27% of 397 females). Males with anti-hantavirus antibodies belonged to the heaviest mass classes ($\overline{X} = 35.48$ g, SE = 7.92, n = 70 of anti-hantavirus antibodies males vs. $\overline{X} = 26.38$ g, SE = 8.22, n = 554 of negatives ones). Abundance of males ($\overline{X} = 58.66$, SE = 14.24) was signif-

icantly higher ($\chi^2 = 29.79$; df = 5; $p < 0.001$) than that of females ($\overline{X} = 38.92$, SE = 9.24). Moreover, scars or wounds were observed only in 18% of infected males and in 29% of infected females.

Discussion

Many rodent species demonstrate distinct local habitat preferences and temporal variation in abundance, which may have practical implications for disease transmission as well as for reservoir management (Mills, 1999). Our study demonstrates that host population and hantavirus infection prevalence varies among habitat types and over time in Southern Argentina, which may influence the risk of human exposure.

Considerable variations in *O. longicaudatus* trap success in brush and forest habitats over time indicate temporal changes in rodent population density. We recorded

Table 2. Percentage of trap lines where *O. longicaudatus* with anti-hantavirus antibodies were captured, by habitat and year in Cholila (2003–2006)

Year/habitat	2003	2004	2005	2006	Total
Forest (294 sites)	11.4	1.1	6	2.8	4.5
Brush (192 sites)	20	18.5	13.6	28.6	16.7
Pasture (294 sites)	2.3	0	0	1.4	0.7
Peridomestic (294 sites)	4.8	0	2.1	1.4	1.6
Total	8.6	3.1	4.2	5.4	4.8

annual and interannual differences in population density both in forest and brush habitats, which is consistent with other published studies in Argentina (Guthmann et al., 1997; Calderón et al., 1999; Cantoni et al., 2001; Piudo et al., 2005) and Chile (Murúa et al., 1996; Murúa and Briones, 2005). Similarly, *O. longicaudatus* is most commonly found in brush and forest habitats, also consonant with other published reports (Pearson and Pearson, 1982; Pearson, 1983; Kelt et al., 1994; Monjeau et al., 1998; González et al., 2000; Pardiñas et al., 2000; Cantoni et al., 2001; Pearson, 2002; Lozada et al., 2000; Pardiñas et al., 2003; Piudo et al., 2005; Mills et al., 2007) about strong habitat selectivity of this species by brush and forest habitats. Considering that environmental variables can affect the population abundance of *O. longicaudatus*, it is valid to suppose that the observed abundance differences among habitat types and seasons could be associated with those environmental differences. In this sense, Pearson and Pearson (1982) suggest that *O. longicaudatus* prefer moist areas with abundant cover. Moreover, Lozada et al. (2000) point out that this species responds to structural components of its environment on a small resolution scale, and Murúa and González (1982) suggest that *O. longicaudatus* selects microsites with high foliage density and thick understory because the foliage offer protection from the horizontal view of predators. Our results also could be a consequence of the methodological approach, because the removal trapping procedure used is considered an invasive technique that could alter the population structure (Kelt et al., 1994). However, considering that each season traplines were placed in different sites and that the distance among them was > 200 m, we could assume that there is very little or no methodological effect on the analyses and results obtained.

Several studies have indicated that the presence and abundance of antibody-positive rodents are not evenly distributed between and within habitats (Mills et al., 1997; Kuenzi et al., 1999; Piudo et al., 2005; Mills et al., 2007). We trapped antibody-positive *O. longicaudatus* in all habitats in variable number of trap sites by season. When high population levels occur, crowding may lead to an increase in intraspecific contacts and virus transmission events (Mills, 1999; Yates et al., 2002). Rodent density may be a relevant parameter to describe hantavirus dynamics in rodent populations. Autumn peaks in population density and high numbers of antibody-positive animals in spring (Figs. 2, 3) suggest a delayed-density-dependent prevalence of infection, which was observed by Niklasson et al. (1995) in *Clethrionomys glareolus*.

Simplification of ecosystems may result in increased viral transmission among rodents and consequently increased risk to humans (Mills, 2005). In northern, central, and some southern areas of Argentina, trap success values for hantavirus host species in peridomestic rural sites were similar or higher than those in open fields represented by other rural sites (Calderón et al., 1999; Piudo et al., 2005), suggesting that the higher risk would be linked to peridomestic settings. Nevertheless, in southern areas we registered a higher trap success and higher numbers of infected animals in natural, relatively undisturbed areas than in urban and periurban ones, in agreement with Cantoni et al. (2001). Moreover, Lázaro et al. (2007) observed no evidence of domestic rodent infestation in some places and no serologic reactivity was detected in rodents captured in some peridomestic habitats. In our study the condition that anthropogenic activity simplified the rodent community was evident, but it seems that it did not favor an increase in viral transmission, as measured by antibody prevalence.

The appearance and disappearance of antibody-positive individuals in some habitat types may suggest that AND virus persists in some habitat refuges, such as forest and brush, and periodically spreads to others, such as peridomestic and pasture. Determining refuges for host population and pathogen transmission in the regional landscape could be a key to develop accurate models for predicting HPS outbreaks (Yates et al., 2002). This study suggests that risk of human exposure to AND virus may be associated with host and pathogen dynamics in brush and forest habitats.

The overall prevalence of anti-hantavirus antibodies varied considerably among other wild rodents captured in Cholila. *Abrothrix olivaceus*, *A. longipilis*, and the phyllotine *Loxodontomys micropus* also have been recorded as hantavirus antibody-positive in other localities in the southern region of Argentina (Cantoni et al., 2001; Piudo et al., 2005; Padula et al., 2004). It is possible that infection in these species may be due to an overflow of the virus from *O. longicaudatus*. Transient and/or spillover infections from the primary hosts into other species occur where spatial and temporal range overlap has been observed (Childs et al., 1994; Pavletic, 2000). Childs et al. (1994), Mills et al. (1997), and Abbott et al. (1999) have suggested that high rodent densities and/or increased interspecific interactions may provide opportunities for spillover to other rodent species.

A positive association between number of antibody-positive individuals and bodyweight suggests that older

animals were more frequently infected than younger. Also male rodents were more frequently infected than females, suggesting that hantavirus may be maintained by horizontal transmission (Mills et al., 1997, 1998; Kuenzi et al., 1999). Association of scars or wounds with the presence of hantavirus antibody has been used to suggest that intraspecific agonistic encounters during the reproductive period is a mechanism of hantavirus transmission within host populations (Mills, 1999; Douglas et al., 2007). Douglas et al. (2007) did not find any association between seroconversion and the acquisition of scars in *Peromyscus maniculatus*, due to the small sample size of deer mice that seroconverted from one trapping session to the next. Some studies have suggested that the frequent association between scars and antibody prevalence may be the result of a postinfection phenomenon (Glass et al., 1988; Calisher et al., 1999; Douglas et al., 2001; Hinson et al., 2004; Klein et al., 2004). Douglas et al. (2007) proposed that both wounding and seroconversion might be related to a third variable, such as population density, which might result in increased aggression and increased transmission but through a mechanism (e.g., environmental contamination) that might be independent of aggression. Calisher et al. (2007) recorded that prevalence seemed to reach a peak much earlier in deer mice with visible wounds than in those for which no wounds were detected, possibly indicating that aggression is not the only mechanism of transmission of SNV among deer mice. The lack of a positive association between scars and infection found in this study suggests that intraspecific aggression is not a common means of AND transmission among *O. longicaudatus* in Argentina.

Oligoryzomys longicaudatus was the most common species captured in the assemblage, being more abundant in relatively undisturbed environments (brush and forests) than in anthropogenically modified environments (peridomestic settings and pasture). Seasonal variation in RDI of *O. longicaudatus* also was observed. Although antibody-positive *O. longicaudatus* individuals were captured in all habitats there was a significant degree of heterogeneity between habitat types (with greatest antibody prevalence in brush habitats) and between sexes and age classes (higher prevalence in the heaviest males). Moreover, not only there was a greater prevalence in brush habitat but also a greater number of positive trap sites. Our results suggest a need to consider those possible times and places of hantavirus transmission to humans in Southern Argentina to identify areas of increased risk. Further characterization of habitat refuges for reservoir hosts, which cause HPS, will be important in development of more accurate models to predict HPS outbreaks.

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REFERENCES

Abbott KD, Ksiazek TG, Mills JN (1999) Long-term hantavirus persistence in rodent populations in central Arizona. *Emerging Infectious Diseases* 5:8–18

Byers CR, Steinhorst RK, Krausman PR (1984) Clarification of a technique for analysis of utilization-availability data. *The Journal of Wild-life Management* 48:1050–1053

Cabrera AL (1976) Regiones fitogeográficas argentinas. Enciclopedia Argentina de Agricultura y Jardinería, Tomo II. Buenos Aires: Editorial ACME, 85 pp

Cabrera AL, Willink A (1980) Biogeografía de América Latina. Serie de Biología, monografía No. 13, O.E.A. 2ª edición corregida, 122 pp

Calderón G, Pini N, Bolpe J, Levis S, Mills J, Segura E, Guthmann N, et al. (1999) Hantavirus reservoir hosts associated with peridomestic habitats in Argentina. *Emerging Infectious Diseases* 6:792–797

Calisher CH, Sweeney W, Mills JN, Beaty BJ (1999) Natural history of Sin Nombre virus in western Colorado. *Emerging Infectious Diseases* 5:126–134

Calisher CH, Wagoner KD, Amman BR, Root JJ, et al. (2007) Demographic factors associated with prevalence of antibody to Sin Nombre virus in deer mice in the western United States. *Journal of Wildlife Diseases* 43:1–11

Cantoni G, Padula P, Calderón G, Mills J, Herrero E, et al. (2001) Seasonal variation in prevalence of antibody to hantaviruses in rodents from southern Argentina. *Tropical Medicine and International Health* 6:811–816

Castillo E, Priotto J, Ambrosio AM, Provensal MC, et al. (2003) Commensal and wild rodents in an urban area of Argentina. *International Biodeterioration and Biodegradation* 52:135–141

Childs JE, Ksiazek TG, Spiropoulou CF, Krebs JW, Morzunov S, Maupin GO, et al. (1994) Serologic and genetic identification of *Peromyscus maniculatus* as the primary rodent reservoir for a new hantavirus in the southwestern United States. *Journal of Infectious Diseases* 169:1271–1280

Debrot S (1981) Trophic relations between stoat (*Mustela erminea*) and its prey, mainly the water vole (*Arvicola terrestris scherman*). In: *Worldwide Furbearer Conference Proceedings*,

Chapman JA, Pursley D (editors), Frostburg, MD, pp 1259–1289

Douglas RJ, Wilson T, Semmens WJ, et al. (2001) Longitudinal studies of Sin Nombre virus in deer mouse-dominated ecosystems of Montana. *American Journal of Tropical Medicine and Hygiene* 65:333–392

Douglas RJ, Calisher CH, Wagoner KD, Mills JN (2007) Sin Nombre virus infection of deer mice in Montana: characteristics of newly infected mice, incidence, and temporal pattern of infection. *Journal of Wildlife Diseases* 43:12–22

Enría DA, Pinheiro F (2000) Rodent-borne emerging viral zoonosis: hemorrhagic fevers and hantavirus infections in South America. In: *Infectious Disease Clinics of North America. Emerging and Re-emerging Diseases in Latin America*, Gotuzzo E, Istúriz R (editors), Vol. 14(1), pp. 167–184

Enría D, Levis S (2004) Zoonosis virales emergentes: las infecciones por hantavirus. *Revue Scientifique et Technique (International Office of Epizootics)* 23(2):595–611

Glass GE (1997) Hantaviruses. *Current Opinion in Infectious Diseases* 10:362–366

Glass GE, Childs JE, Korch GW, Leduc JW (1988) Association of intraspecific wounding with hantaviral infection in wild rats (*Rattus novegicus*). *Epidemiology and Infection* 101:459–472

González LA, Murúa R, Jofré C (2000) Habitat utilization of two muroid species in relation to population outbreaks in southern temperate forest of Chile. *Revista Chilena de Historia Natural* 73:3

González Della Valle M, Edelstein A, Miguel S, et al. (2002) Andes virus associated with HPS in Northern Argentina and determination of the precise site of infection. *Journal of American Tropical Medicine and Hygiene* 66:713–720

González-Ittig R, Salazar-Bravo J, Polop JJ, Gardenal CN (2008) Isolation and characterization of microsatellite markers in *Oligoryzomys longicaudatus* (Muridae, Sigmodontinae, Oryzomini), the natural reservoir of genotype Andes hantavirus. *Molecular Ecology Resources* 8:1466–1468. doi:10.1111/j.1755-0998.2008.02231.x

Guthmann N, Lozada M, Mongeau JA, Heinemann MK (1997) Population dynamics of five sigmodontine rodents of northwestern Patagonia. *Acta Theriologica* 42(2):143–152

Hinson ER, Shone SM, Zink MC, Glass GE, Klein SL (2004) Wounding: the primary mode of Seoul virus transmission among male Norway rats. *American Journal of Tropical Medicine and Hygiene* 70:310–317

Kelt DA, Meserve PL, Lang BK (1994) Quantitative habitat associations of small mammals along in a temperate rainforest in southern Chile: empirical patterns and the importance of ecological scale. *Journal of Mammalogy* 76:562–568

Khan A, Spiropoulou CF, Morzunov S, et al. (1995) Fatal illness associated with a new hantavirus in Louisiana. *Journal of Medical Virology* 46:281–286

Klein SL, Zink MC, Glass GE (2004) Seoul virus infection increases aggressive behaviour in male Norwa rats. *Animal Behaviour* 67:421–429

Kuenzi AJ, Morrison ML, Swann DE, Hardy PC, Downard GT (1999) A longitudinal study of Sin Nombre virus prevalence in rodents, Southwestern Arizona. *Emerging Infectious Diseases* 5:113–117

Larrieu E, Herrero E, García-Cachau M, Labanchi JL, Manzini S, et al. (2003) Seroprevalencia de Hantavirus en roedores y casos humanos en el sur de Argentina. *Revista Brasilera de Epidemiología* 6:68–75

Lázaro M, Cantoni GE, Calani LM, Resa AJ, Herrero ER, et al. (2007) Clusters of Hantavirus Infection, Southern Argentina. *Emerging Infectious Diseases* 13:104–110

León RJC, Bran D, Collantes M, Paruelo JM, Soriano A (1998) Grandes unidades de vegetación de la Patagonia extra andina. En: *Ecosistemas patagónicos*, Oesterheld M, Aguiar MR, Paruelo JM (eds). Ecología Austral. Publicación de la Asociación Argentina de Ecología, Vol. 8(2), pp. 125–144

Levis S, Briggiler AM, Cacass M, et al. (1995) Emergence of Hantavirus pulmonary syndrome in Argentina. In: *Program and Abstracts of 44th Annual Meeting of the American Society of Tropical Medicine and Hygiene*, San Antonio

Levis SC, Morzunov SP, Rowe JE, Enría DA, Pini N, et al. (1998) Genetic diversity and epidemiology of hantaviruses in Argentina. *Journal of Infectious Disease* 177:529–538

Levis SC, Garcia J, Pini N, Calderón G, Ramírez J, Bravo D, St Jeor S, et al. (2004) Hantavirus pulmonary syndrome in northwestern Argentina: circulation of Laguna Negra virus associated to *Calomys callosus*. *American Journal of Tropical Medicine and Hygiene* 71(5):658–663

López N, Padula P, Rossi C, Lázaro ME, Franze-Fernández MT (1996) Genetic identification of a new hantavirus causing severe pulmonary syndrome in Argentina. *Virology* 220:223–226

Lozada M, Guthmann N, Baccala N (2000) Microhabitat selection of five sigmodontine rodents in a forest-steppe transition zone in northwestern Patagonia. *Studies on Neotropical Fauna and Environment* 35:85–90

Martinez VP, Colavecchia S, García Alay M, et al. (2001) Síndrome Pulmonar por Hantavirus en la Provincia de Buenos Aires. *Medicina* 61:147–156

Meserve PL, Le Boulengé E (1987) Population dynamics and ecology of small mammals in the northern Chilean semiarid region. *Fieldiana Zoology New Series* 39:413–431

Meserve PL, Gutiérrez JR, Yunger JA, Contreras LC, Jaksic FM (1996) Role of biotic interactions in a small mammal assemblage in semiarid Chile. *Ecology* 77:133–148

Mills JN (1999) The role of rodents in emerging human disease: examples from the hantaviruses and arenaviruses. In: *Ecologically-Based Rodent Management*, Singleton GR, Hinds LA, Leirs H, Zhang Z (editors), Canberra, Australia: Arrawang Communication Group, pp 134–160

Mills JN (2005) Regulation of rodent-borne viruses in the natural host: implications for human disease. *Archives of Virology* 19:45–57

Mills JM, Ellis BA, Mckee KT, Maiztegui JI, Childs JE (1991) Habitat associations and relative densities of rodent populations in cultivated areas of central Argentina. *Journal of Mammalogy* 72:471–479

Mills JN, Yates TL, Childs JE, Parmenter RR, Ksiazek TG, et al. (1995) Guidelines for working with rodents potential infected with hantavirus. *Journal of Mammalogy* 76:716–722

Mills JN, Ksiazed TG, Ellis BS, Rollin PE, Nichols ST, Yates TL, Gannon WL, et al. (1997) Patterns of association with host and habitat: antibody reactive with Sin Nombre virus in small mammals in the major biotic communities of the southwestern United States. *American Journal of Tropical Medicine and Hygiene* 56:273–284

Mills JN, Johnson JM, Ksiazek TG, Ellis BA, Rollin PE, Yates TL, Mann MO, et al. (1998) A survey of hantavirus antibody in small-mammal populations in selected United States National Parks. *American Journal of Tropical Medicine and Hygiene* 58:525–532

Mills JN, Schmidt K, Ellis BA, Calderón G, Enría DA, Ksiazek TG (2007) A longitudinal study of hantavirus infection in three

sympatric reservoir species in agroecosystems on the Argentine Pampa. *Vector-Borne and Zoonotic Diseases* 7:229–240

Monjeau JA, Birney EC, Ghermandi L, Sikes RS, Margutti L, Phillips CJ (1998) Plants, small mammals, and the hierarchical landscape classifications of Patagonia. *Landscape Ecology* 13:285–306

Morzunov S, Feldmann H, Spiropoulou CF, et al. (1995) A newly recognized virus associated with a fatal case of hantavirus pulmonary syndrome in Louisiana. *Journal of Virology* 69:1980–1983

Murúa R, Briones M (2005) Abundance of the sigmodont mouse *Oligoryzomys longicaudatus* and patterns of tree seeding in Chilean temperate forest. *Mammalian Biology* 70:321–326

Murúa R, González LA (1982) Microhabitat selection in two Chilean cricetid rodents. *Oecologia* 52:12–15

Murúa R, González LA (1986) Regulation of numbers in two Neotropical rodent species in southern Chile. *Revista Chilena de Historia Natural* 59:193–200

Murúa R, González LA, Meserve PL (1996) Population ecology of *Oryzomys longicaudatus philippii* (Rodentia: Cricetidae) in southern Chile. *Journal of Animal Ecology* 55:281–293

Nichol ST, Spiropoulou CF, Morzunov S, et al. (1993) Genetic identification of a hantavirus associated with an outbreak of acute respiratory illness. *Science* 262:914–917

Niklasson B, Hornfeldt B, Lundkvist A, Bjorsten S, Lê Duc J (1995) Temporal dynamics of Puumala vírus antibody prevalence in voles and of nephropathia epidemic incidence in humans. *American Journal of Tropical Medicine and Hygiene* 53:134–140

Padula PJ, Colavecchia SB, Martínez VP, Gonzalez Della Valle MO, Edelstein A, et al. (2000) Genetic diversity, distribution, and serological features of hantavirus infection in five countries in South America. *Journal of Clinical Microbiology* 38:3029–3035

Padula P, Figueroa R, Navarrete M, Pizarro E, Cadiz R, et al. (2004) Transmission study of Andes hantavirus infection in wild sigmodontine rodents. *Journal of Virology* 78:11972–11979

Pardiñas UFJ, Moreira G, García-Esponda C, De Santis LJM (2000) Deterioro ambiental y micromamíferos durante el Holoceno en el nordeste de la estepa patagónica (Argentina). *Revista Chilena de Historia Natural* 72:541–556

Pardiñas UFJ, Teta P, Cirignoli S, Podestá DH (2003) Micromamíferos (Didelphimorphia y Rodentia) de norpatagonia extra andina, Argentina: taxonomía alfa y biogeografía. *Mastozoología Neotropical* 10:69–113

Pavletic BC (2000) Hantavirus: su distribución geográfica entre los roedores silvestres de Chile. *Revista Chilena de Infectología* 17:186–196

Pearson OP (1983) Characteristics of mammalian faunas from forests in Patagonia, southern Argentina. *Journal of Mammalogy* 64:476–492

Pearson OP (2002) A perplexing outbreak of mice in Patagonia, Argentina. *Studies on Neotropical Fauna and Environment* 37:187–200

Pearson OP, Pearson AK (1982) Ecology and biogeography of the southern rainforest of Argentina. In: *Mammalian Biology in South America: Special Publications Series*, Mares MA, Genoways HH (editors), Linesville, USA: Pymatuning Laboratory of Ecology, University of Pittsburgh, pp. 129–142

Piudo L, Monteverde M, González Capria S, Padula P, Carmanchahi P (2005) Distribution and abundance of sigmodontine rodents in relation to hantavirus in Neuquén, Argentina. *Journal of Vector Ecology* 30:119–125

Porcasi X, Calderón GE, Lamfri M, Scavuzzo M, Sabattini MS, Polop JJ (2005) Predictive distribution maps of rodent reservoir species of zoonoses in Southern America. *Mastozoología Neotropical* 12:199–216

Riera LM, Parisi MN, Seijo A, Pini NC, Sabattini M, Enría D (1994) Infección por Leptospira y virus Hantaan en pacientes con fiebre hemorrágica en el área endémica de FHA. I Congreso Interamericano de Infectología. Córdoba, Argentina: Libro de resúmenes, p. 148

Rollin PE, Ksiazek TG, Elliott LH, et al. (1995) Isolation of Black Creek Canal virus, a new hantavirus from *Sigmodon hispidus* in Florida. *Journal of Medical Virology* 46:35–39

Saucy F (1994) Density dependence in time series of the fossorial form of the water vole, *Arvicola terrestris*. *Oikos* 71:381–392

Schmaljhon C, Hjelle B (1997) Hantaviruses: a global disease problem. *Emerging Infectious Diseases* 3:95–104

Sosa Estaini S, Martinez PV, Gonzalez Della Valle M, et al. (2002) Hantavirus in human and rodent population in an endemic area of hantavirus pulmonary syndrome in Argentina. *Medicina* 62:1–8

Yates TL, Mills JN, Parmenter CA, Ksiazek TG, et al. (2002) The ecology and evolutionary history of an emergent disease: hantavirus pulmonary syndrome. *BioScience* 52:989–998

Young JC, Mills JN, Enría DA, et al. (1998) New World hantaviruses. *British Medical Bulletin* 54:659–673