Hantavirus Infection and Habitat Associations among Rodent Populations in Agroecosystems of Panama: Implications for Human Disease Risk

Aníbal G. Armién,* Blas Armién, Frederick Koster, Juan M. Pascale, Mario Avila, Publio Gonzalez, Manuel de la Cruz, Yamitzel Zaldivar, Yaxelis Mendoza, Fernando Gracia, Brian Hjelle, Sang-Joon Lee, Terry L. Yates,† and Jorge Salazar-Bravo

Department of Population Medicine, College of Veterinary Medicine, University of Minnesota, Saint Paul, Minnesota, Instituto Conmemorativo Gorgas de Estudios de la Salud, Panama City, Panama; Ministry of Health, Herrera Province, Panama; Lovelace Respiratory Research Institute, Albuquerque, New Mexico; Hospital Santo Tomas, Panama City, Panama; Department of Pathology, School of Medicine, University of New Mexico, Albuquerque, New Mexico; Division of Epidemiology and Biostatistics, Department of Internal Medicine, University of New Mexico, Albuquerque, New Mexico; Center for Epidemiology and Zoonoses, Texas Tech University, Lubbock, Texas

Abstract.   Hantavirus cardiopulmonary syndrome (HCPS), which is caused by infection with Choclo virus, is uncommon in Panama, yet seropositivity among rural residents is as high as 60%. To clarify the environmental risk factors favoring rodent-to-human transmission, we tested serum from 3,067 rodents captured over a five-year period for antibodies against recombinant N protein of hantavirus by enzyme immunoassay and strip immunoblot. Among 220 seropositive rodents, *Oligoryzomys fulvescens*, the reservoir of Choclo virus, had the highest overall seroprevalence (23.5%); more abundant rodents (*Zygodontomys brevicauda* and *Sigmodon hirsutus*) had lower seroprevalences. In the mixed (combined modern and traditional) productive agroecosystem, the highest seroprevalence was among *O. fulvescens* captured in residences and in crops grown within 40 meters of a residence, with significantly lower seroprevalence in adjacent pasture and non-productive vegetation. Thus, crop habitats may serve as refugia for invasion into adjacent human residences and suggests several interventions to reduce human infection.

INTRODUCTION

Hantavirus cardiopulmonary syndrome (HCPS) is an acute and often fatal febrile disease caused by enveloped, trisegmented, negative-strand RNA viruses of the family *Bunyaviridae* and genus *Hantavirus*. This syndrome is characterized by increase vascular permeability, atypical interstitial pneumonitis, and acute cardiac dysfunction. Since the first description of HCPS in the southwestern United States in 1993, novel New World hantaviruses and their specific rodent reservoirs have been documented in most regions of the Americas.[1–6]

Each hantavirus is typically associated with a single species of murid rodent host in which it establishes a chronic infection that involves shedding of the infectious virus in bodily secretions and excretions. Studies in rodent models suggest that hantavirus may be transmitted principally among rodents by saliva or saliva aerosols.[7,8] Direct bloodborne transmission by biting and fighting may be an important mode of infection[9] It is believed to be transmitted to humans by inhalation of aerosolized virus in association with rodent excreta. Person-to-person transmission has been described only for Andes virus,[10,11] and there is no evidence for person-to-person transmission in Panama. Peridomestic environments with active rodent infestations may present the greatest risk for human infection.[9,12–15] Risk of transmission to persons is largely defined by the rodent reservoirs' geographic distributions, although within these regions, risk also varies with the ecology of the rodent species and human contact within their habitats.[16–20]

In Central America, HCPS was first reported in the Azuero Peninsula of Panama. In the HCPS outbreak of 1999–2000, a novel human-pathogenic hantavirus (Choclo virus) and its rodent reservoir (*Oligoryzomys fulvescens*) were identified in peridomestic environments.[21–23] In the investigation, differences were found in small mammal community structure between case sites and a control site, suggesting that human activities coupled with environmental factors may have combined to cause an increased risk of HCPS to residents in the Azuero Peninsula.[23] From six reservoir species identified in Panama, a geographic focus of hantavirus infection in rodents was evident, with Choclo and Calabazo viruses circulating in rodent populations in the Azuero Peninsula.[24] The short-tailed cane mouse (*Zygodontomys brevicauda*), the host of Calabazo virus, was found to be the most abundant rodent and the dominant species on the flat land of Azuero Peninsula.[25]

In Panama, all HCPS appears to be caused by Choclo virus[21,26] with only 106 cases and 22 deaths (21.0%) reported to the present (Armién B, unpublished data). In contrast to most hantavirus-endemic regions, however, a high prevalence of antibody to hantavirus (up to 60%) is found in residents of the endemic agricultural region of central Panama (Armién B, unpublished data). Similar to other America hantaviruses, transmission of Choclo virus appears to be predominantly in peridomestic habitats.[20,26–30] The high seroprevalence of hantavirus antibody in rodents as well as humans permits a more detailed examination of microhabitats within the peridomestic area where infected rodents and humans interact. We hypothesized that in agroecosystems in Panama, specific crop microhabitats near human habitation provided high-risk sites for human infection. This study focuses on habitat associations of hantavirus-infected rodents; a longitudinal study and climate-driven fluctuations in rodent and human infections are presented elsewhere.

MATERIALS AND METHODS

Trapping and study sites. Our sampling was conducted in 35 localities in central section of western Panama (Figure 1). There is a rainy season from May through December and a dry season from January through April. The lowlands of central-western Panama are heavily populated and much of the original deciduous forest has been converted to an

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*Address correspondence to Aníbal G. Armién, Department of Population Medicine, College of Veterinary Medicine, University of Minnesota, Saint Paul, MN 55108. E-mail: armie001@umn.edu
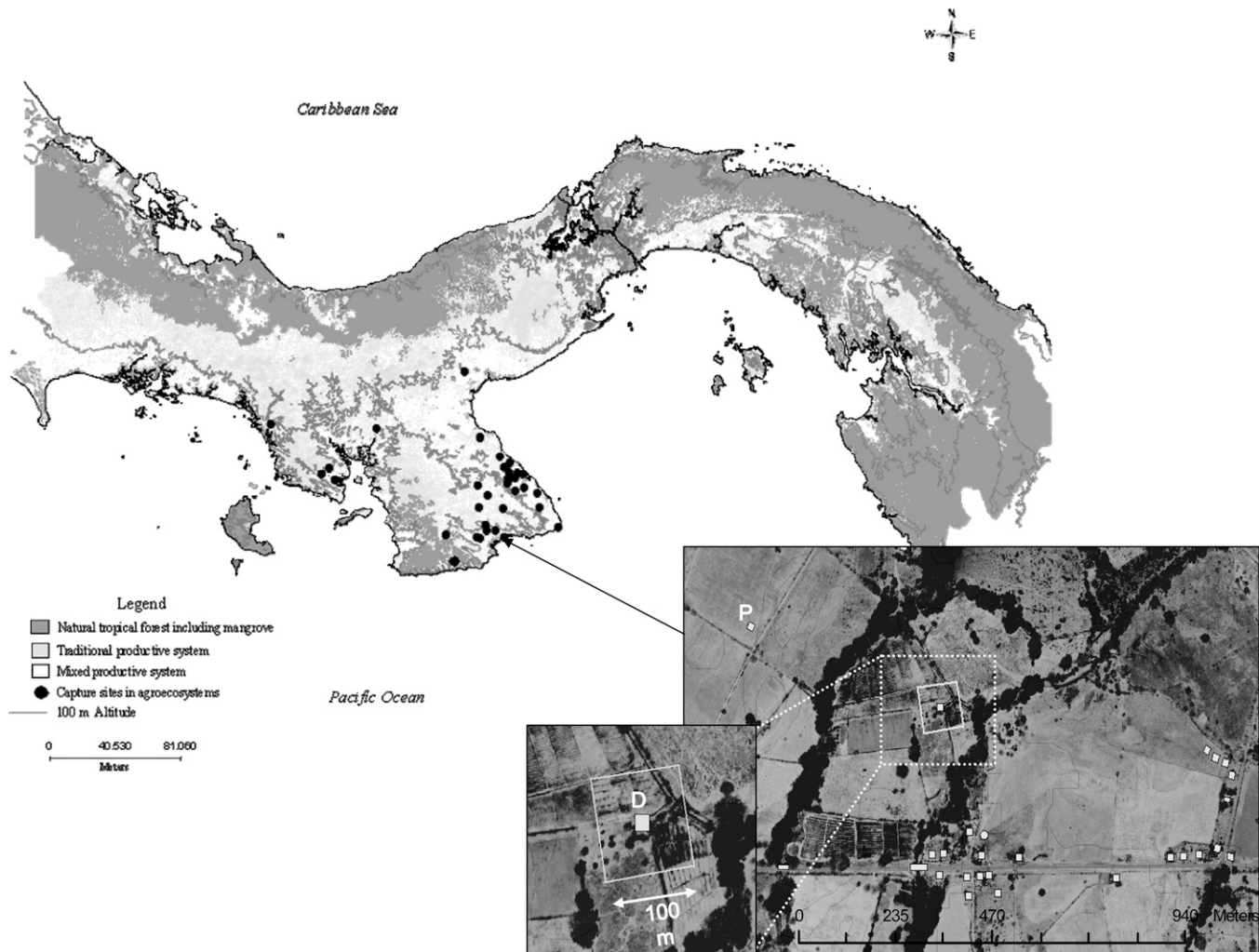† Deceased.

FIGURE 1.   Map of ecosystems and sampling localities in Panama, 2002–2006. Aerial photography of the hantavirus cardiopulmonary syndrome–endemic community of Agua Buena in the Tonosi Valley of the Azuero Peninsula of Panama. The peridomestic area (P) is characterized by dominant mechanized rice plantation and pasture. Strips of riparian vegetation follow a series of ravines composed of narrow corridors (5–75 meters in width) associated with planting vegetables and complexes matrix of residences (white squares). Inset: Magnification of the domestic area (D) showing environments inside and outside the habitation where a 100 trap station was placed. Source: Map of vegetation cover of the Republic of Panama. Satellite images LandSat TM5-TM7, Panamanian National Environment Authority (ANAM), 2000.

agroecosystem. Small fragments of secondary dry deciduous forests exist primarily in the lowlands, large areas of evergreen forests predominate in higher elevations, and mangrove vegetation is locally abundant along the coast.

In the agroecosystems of central-western Panama, 60% of the land area is covered by agricultural vegetation located on flat to sloping topography with good to poor quality soils. Productive systems in Panama are defined in terms of land use, topography, and relative density of native second-growth vegetation cover (Figure 1) as either of two categories according to agricultural intensification.[31] The predominant category is the mixed productive system (MPS) (combined modern and traditional productive systems) characterized by small to large scale mechanized agriculture on lowland with small to large scale irrigation system, semi-extensive livestock grazing and less than 10% of native shrub and mature second-growth vegetation cover. Human habitations are closely adjacent to subsistence as well as mechanized cropland (Figure 1). The second category is the traditional productive system (TPS) located on predominantly sloped topography with extensive livestock grazing, subsistence

agriculture, and 10–40% covered with native shrub and mature second-growth vegetation on the remaining fragments.

Within these two categories of productive systems, we trapped rodents in two distinct environments, defined as domestic and peridomestic habitats. The domestic habitat included the area of family activities within (intradomestic) and outside (paradomestic) the habitation, and extended in general up to 40 meters from the perimeter of the residence. The paradomestic microhabitat is defined as the areas immediately outside human habitations consisted typically of yard that include patio and ornamental garden, weeds, subsistence crops plantation (corn, sugar cane, vegetables) and livestock barns. Occasionally small areas of mechanized plantations were located in the paradomestic area. The peridomestic habitat is defined as the area of human activity more than 40 meters from the perimeter of residences and consisted of small to large scale mechanized plantations of rice, corn, sugar cane, vegetables, cultivated wood, cultivated grass, native grassland (e.g., *Hyparrhenia rufa*) used for cattle, as well as small fragments of subsistence cultivation.

Small-mammal sampling. Sherman live traps (model LFATDG; H. B. Sherman Traps, Inc., Tallahassee, FL) were set from January 2002 through December 2006 in 35 localities of central-western Panama, with 79.0% of the trapping effort concentrated on the Azuero Peninsula. Traps were baited with a mixture of crunchy peanut butter and cracked corn, or a combination of rolled oats, birdseed, molasses, and vanilla extract. Grids of 100 traps (10 columns by 10 rows set at 10-meter intervals) were established in microhabitats (i.e., vegetation, crop of the season, human habitation) in domestic and peridomestic areas. In 1.3% of the trapping effort, 100 traps were randomly placed in some domestic and peridomestic areas. Trapping in each site was conducted for three consecutive nights during the dry and wet seasons throughout the five years of the study. A total of 80.9% (61,405) of the trapping effort was concentrated in the MPS, whereas 19.1% (14,528) was performed in the TPS. Description of the microhabitats was consistently recorded.

Mammals were handled according to recommendations by Mills and others.[32] Blood was obtained from the retro-orbital sinus using heparinized capillary tubes. The animals were killed with inhaled methoxyflurane (Pitman-Moore, Mundelein, IL). Individual field catalog numbers were assigned to each animal. Data collected for all individuals captured included trap location, weight, and standard body measurements (length of body, tail, hind foot, and ear). Data on sex and reproductive condition were determined based on the dimension and position of male testes and, in females, based on nipple size, state of lactation, and/or when the vagina was open. The approximate age was estimated based on coat characteristics, body dimensions, mass, and reproductive condition. Rodents were identified in the field using existing keys.[33,34] For the known reservoir species (*Oligoryzomys fulvescens*, *Zygodontomys brevicauda*, and *Sigmodon hirsutus*), individuals were assigned to body mass classes chosen to correspond to subjective maturational events based on standardized field data.

For *O. fulvescens*, the body mass classes were juvenile (class I, < 6.0 grams; class II, 6–7.9 grams); young adult (class III, 8–9.9 grams; class IV, 10–11.9 grams); Adult (class V, 12–13.9 grams; class VI, 14–15.9 grams; class VII, ≥ 16.0 grams). For *Z. brevicauda*, the body mass classes were juvenile (class I < 10.0 grams; class II, 10–19.9 grams); young adult (class III, 20–29.9 grams; class IV, 30–39.9 grams); adult (class V, 40–49.9 grams; class VI, 50–59.9 grams; class VII, ≥ 60 grams). For *S. hirsutus*, the body mass classes were juvenile (class I, < 15.0 grams; class II, 15–29.9 grams); young adult (class III, 30–44.9 grams; class IV, 45–59.9 grams); adult (class V, 60–74.9 grams; class VI, 75–89.9 grams; class VII, ≥ 90 grams).

Ectoparasites and presence and nature of external wounds on the head, ears, body, legs, and tail were recorded. Blood and samples of the spleen, liver, kidneys, heart, and lungs were collected in separate, labeled cryovials using clean sterilized instruments for each animal. All biologic samples were immediately placed into liquid nitrogen. After processing, the carcasses were placed either directly into 80% ethanol or into 10% formalin for 3 days, followed by immersion in 70% ethanol for long-term preservation. All animals were deposited in the Museum of Southwestern Biology (University of New Mexico, Albuquerque, NM) or the Gorgas Memorial Institute (Panama City, Panama). Permits to collect and export small mammals were provided by the National Environment Authority (Panama City, Panama).

Serologic analysis. Animals were tested by strip immunoblot for IgG containing a recombinant N protein of the CC106 strain of Sin Nombre virus and used as described.[35] Seropositivity was confirmed by reverse transcription–polymerase chain reaction (RT-PCR) and sequencing of amplimers from RNA tissue extracts of 10 seropositive *O. fulvescens* and 14 seropositive *Z. brevicauda* specimens, as Choclo and Calabazo viruses, respectively.

Data analyses. Data were transferred from field collection forms to a database (Epi Info Version 6.04d, Centers for Disease Control and Prevention, Atlanta, GA) for statistical analyses using StatsDirect Statistical Software Version 2.6.5, 2007 (StatsDirect Software, Altrincham, United Kingdom) and Epi-Info Software. Relative abundance corresponding to trap success was estimated by the number of individual captures per 100 trap-nights, whereas the trap nights were equal to the number of trap sets multiplied by the number of nights.[36]

To account for small expected values of categorical data table, we used Fisher's exact test and corresponding exact *P* values. The observed outcomes are assumed to be independent because captured mammals were not released; thus, we do not have a chance to capture the same mammals again. There may be a certain probability that we still have some correlation between observations caused by transmission. However, we did not perform statistical tests accounting for correlation between individual observations assuming independence for simplicity. We performed comparison studies for proportions (with 95% confidence intervals [CIs]) to examine if we can detect a statistically significant difference with a 5% significance level in the detection of antibodies against hantavirus and in the following pairs of comparisons: same species among habitat and microhabitat (i.e., MPS versus TPS, or domestic versus peridomestic or, intradomestic versus paradomestic or, among vegetation categories of the paradomestic or peridomestic habitats); among rodent species in a single habitat or microhabitat; and among rodent sex, age, and wound status. The statistical significance level has been adjusted for multiple comparisons based on Bonferroni correction when we interpreted our results.

RESULTS

Small-mammal community structure and distribution. During 5 years of trapping, 75,933 effective trap-nights yielded 3,446 individuals belonging to 14 species in 4 rodent families: *Muridae*, *Cricetidae*, *Heteromyidae* and *Echimyidae*. *Zygodontomys brevicauda* (56.0%), *S. hirsutus* (21.3%), *Liomys adspersus* (11.7%), and *O. fulvescens* (9.3%), the reservoir of Choclo virus, were the most abundant species. The remaining 10 species represented 1.7% of all individuals trapped (Supplementary Table 3, available online at www.ajtmh.org). Thirteen species were found in the MPS whereas 9 species were found in the TPS. In the MPS, 13 species were captured, with *Z. brevicauda* (65.5%), *S. hirsutus* (15.6%) the reservoir of a novel hantavirus, and *O. fulvescens* (10.9%) as the dominant species, with a relative abundance in the MPS of 4.7 individuals/100 trap-nights. In the TPS sites, the relative abundance was 3.8 individuals/100 trap-nights. The dominant species were *S. hirsutus* and *L. aspersus* (51.3% and 38.6%, respectively), and *Z. brevicauda* and *O. fulvescens* represented 7.0% and 1.1%, respectively (Supplementary Table 3).

Prevalence of hantavirus antibodies and rodent habitat association. Among 3,067 (89%) individuals tested for hantavirus antibody only three species contained all seropositive rodents (Table 1). *Oligoryzomys fulvescens* the fourth most common rodent in both the MPS and TPS, had the highest percentage of positive individuals (23.5%) compared with 7.8% of *Z. brevicauda*, the most abundant rodent in the MPS and the reservoir of Calabazo virus, and 3.4% of *S. hirsutus*, the most common rodent in the TPS and the reservoir of a novel hantavirus (*S. hirsutus*-associated hantavirus). Virtually all of the antibody-positive *O. fulvescens* (67 of 68) and *Z. brevicauda* (128 of 129) were captured in the MPS. In contrast, more seropositive *S. hirsutus* were captured in the TPS than in the MPS (odds ratio [OR] = 4.92, 95% CI = 1.82–15.42, *P* = 0.0006).

The proportion of seropositive *O. fulvescens* was high in the domestic and peridomestic habitats (18.6% and 27.1%, respectively) (Figure 2). The relative abundance of *O. fulvescens* was greater in the domestic habitat than in the peridomestic habitat, possibly increasing the risk of human contact with Choclo-infected rodents in the home (Figure 2). *Oligoryzomys fulvescens* was more likely to be seropositive than *Z. brevicauda* in peridomestic (OR = 4.29, 95% CI = 2.83–6.44, *P* < 0.0001) and domestic (OR = 2.85, 95% CI = 1.39–5.81, *P* = 0.0020) habitats. Both *Oligoryzomys fulvescens* and *Z. brevicauda* were found commonly inside houses but *O. fulvescens* was more likely to be seropositive (42.9%) inside human habitations (Figure 3).

Comparison of rodent seropositivity in different paradomestic microenvironments (pasture, crops, weeds, and ornamental garden) showed low seropositivity among *O. fulvescens* in pasture (9%), weeds (11%) and ornamental gardens (16%) but high seropositivity in adjacent crops (50%), comparable to the high seropositivity of captures in the habitations (42%) (Figure 3). Density is also a critical factor, reflecting relative abundance of captured rodents; 61.1% (11 of 18) of all antibody-positive *O. fulvescens* in the paradomestic area were captured in ornamental gardens. In contrast to seropositive *O. fulvescens* in certain suitable microenvironments, the seropositivity for *Z. brevicauda* was the same across all microenvironments (Figure 3).

In the peridomestic habitats more distant from the habitations, the proportion of antibody-positive *O. fulvescens*
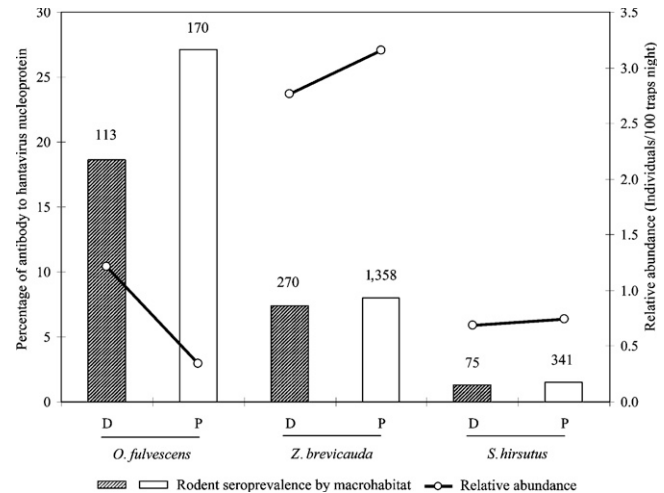

FIGURE 2. Percentage of individuals with antibodies against hantavirus nucleoprotein and relative abundance of rodents capture (individuals/100 traps night) for *Oligoryzomys fulvescens*, *Zygodontomys brevicauda*, and *Sigmodon hirsutus* by domestic (D) and peridomestic (P) habitat in agroecosystems in central-western Panama, 2002–2006. Numbers above each column indicate numbers of individuals tested.

was almost as high as some domestic habitats, with 15.6% in pasture, 28.9% in secondary vegetation, and 32.2% in crops (Supplementary Table 4, available online at www.ajtmh.org). The proportion of seropositive *O. fulvescens* varied from 25.0% in rice to 42.9% in corn (Figure 4), and relative abundance was comparable among each crop, suggesting that *O. fulvescens* had no strong preference for any one crop in spite of its common name, rice rat.

Antibody prevalence in relation to sex, mass class, and wound status. The prevalence of hantavirus antibody was significantly higher in male rodents than in female rodents for *O. fulvescens* (*P* = 0.0107, by Fisher's exact test) and *Z. brevicauda* (*P* < 0.0001, by Fisher's exact test) but not for *S. hirsutus* (Table 2). Seropositive individuals were more frequently adults among *O. fulvescens* (*P* = 0.0006, by Fisher's exact test) and *Z. brevicauda* (*P* < 0.0001, Fisher's by exact test). The prevalence of hantavirus antibody was significantly higher in wounded than unwounded males rodents for both

TABLE 1

Percentage of *Oligoryzomys fulvescens* (*Of*), *Zygodontomys brevicauda* (*Zb*) and *Sigmodon hirsutus* (*Sh*) with antibodies against hantaviruses captured in agroecosystems in central-western Panama, 2002–2006*

Species	Agroecosystems		
	Mixed productive system, % (IgG+/n)†	Traditional productive system, % (IgG+/n)‡	Total % positive (IgG/n)§
O. fulvescens¶	23.7 (67/283)	16.7 (1/6)	23.5 (68/289)
Z. brevicauda#	7.9 (128/1,628)	2.9 (1/35)	7.8 (129/1,663)
*S. hirsutus***	1.4 (6/416)	6.7 (17/253)	3.4 (23/669)
Other species††	0 (0/223)	0 (0/223)	0 (0/446)
No. positive animals of total tested‡‡	7.9 (201/2,550)	3.7 (19/517)	7.2 (220/3,067)
No. species positive	3	3	3
% Species positive	23.1 (3/13)	33.3 (3/9)	21.4 (3/14)

* Fisher's exact test was used to estimate the *P* value. % = percentage of individuals with antibodies against hantavirus nucleoprotein; IgG+ = no. of rodents that were antibody reactive to hantavirus; n = no. of mice for each category.
† *Of* vs. *Zb*, odds ratio (OR) = 3.63, 95% confidence interval (CI) = 2.57–5.10, *P* < 0.0001; *Of* vs. *Sh*, OR = 21.20, 95% CI = 9.00–60.55 *P* < 0.0001; and *Zb* vs. *Sh*, OR = 5.83, 95% CI = 2.58–16.30, *P* < 0.0001.
‡ *Of* vs. *Zb*, OR = 6.80, 95% CI = 0.07–548.82, *P* = 0.2744; *Of* vs. *Sh*, OR = 2.77, 95% CI = 0.06–26.79, *P* = 0.3538; and *Sh* vs. *Zb*, OR = 2.45, 95% CI = 0.36–105.32, *P* = 0.7074.
§ *Of* vs. *Zb*, OR = 3.66, 95% CI = 2.60–5.12, *P* < 0.0001; *Of* vs. *Sh*, OR = 8.60, 95% CI = 5.16–14.86, *P* < 0.0001; and *Sh* vs. *Zb*, OR = 2.36, 95% CI = 1.49–3.89, *P* < 0.0001.
¶ Mixed productive system vs. traditional productive system, OR = 1.55, 95% CI = 0.17–74.43, *P* = 1.0000.
# Mixed productive system vs. traditional productive system, OR = 2.90, 95% CI = 0.48–118.83, *P* = 0.5160.
** Traditional productive system vs. mixed productive system, OR = 4.92, 95% CI = 1.82–15.42, *P* = 0.0006.
†† Other antibody-negative rodent species were included: *Liomys adspersus* (393), *Mus musculus* (28), *Rattus rattus* (10), *Proechimys semispinosus* (2), *Nyctomys sumichrastis* (1), *Oryzomys bolivaris* (1), *Oecomys trinitatis* (2), *Oryzomys couesi* (5) and *Oryzomys talamancae* (4).
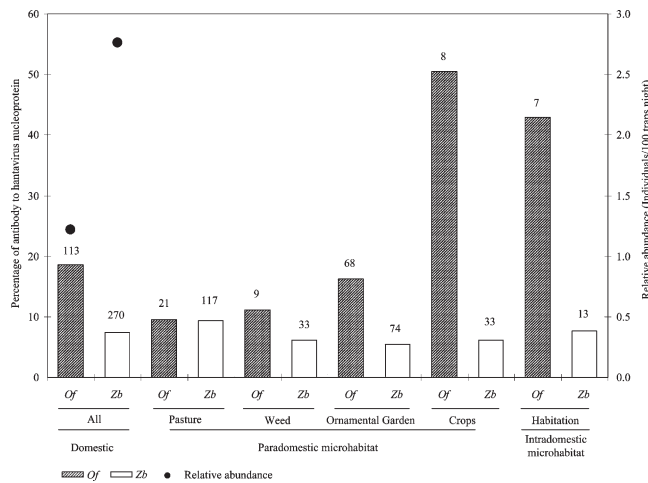‡‡ 89.0% (3,067/3,446) of all captured animals were tested.

FIGURE 3. Percentage of individuals with antibodies against hantavirus nucleoprotein and relative abundance of rodents capture (individuals/100 traps night) for *Oligoryzomys fulvescens* (*Of*) and *Zygodontomys brevicauda* (*Zb*) by vegetation type and environments in domestic area in agroecosystems in central-western Panama, 2002–2006. Numbers above each column indicate numbers of individuals tested.

O. fulvescens (P = 0.0005, by Fisher's exact test) and *Z. brevicauda* (P = 0.0004, by Fisher's exact test). Wounding correlated with larger body mass among wounded males for both species (Supplementary Figure 5, available online at www.ajtmh.org).

DISCUSSION

This study confirms previous findings of evidence of hantavirus infection among rodents in central-western Panama.[21,23] As a consequence of our larger data set and more detailed analyses, a better understanding of the ecology of the reservoir species with implication for human disease risk emerge. Greater numbers of captures found higher seroprevalence than previously reported[24] and increased our ability to correlate seroprevalence with favored habitats. The overall seroprevalence of 23.5% among *O. fulvescens,* host for the human pathogen
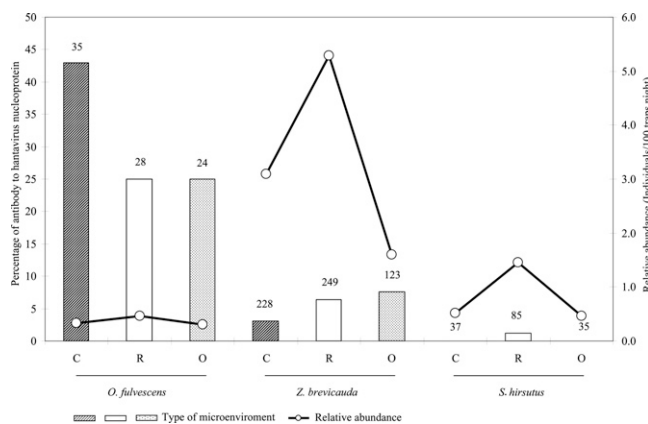

FIGURE 4. Percentage of individuals with antibodies against hantavirus nucleoprotein and relative abundance of rodents capture (individuals/100 traps night) for *Oligoryzomys fulvescens* (*Of*), *Zygodontomys brevicauda*, and *Sigmodon hirsutus* (*Sh*) by crop (Corn [C], Rice [R] and Others [O]) in peridomestic area in agroecosystems in central-western Panama, 2002–2006. Numbers above each column indicate numbers of individuals tested.

Choclo virus, is higher than that reported for most pathogenic hantaviruses in Central and South America.[6,16,20,37,38] The high rodent seroprevalence to Sin Nombre virus in western North America[39–42] is contrasted to the low human seroprevalence of less than 1%. Only the high *Calomys laucha* rodent[20] and human[27] seroprevalences caused by Laguna Negra virus in western Paraguay, where peridomestic infection and MPS predominate, approaches that documented in Panama. Because human seroprevalence on the Azuero Peninsula is high, ranging from 16% to 60%, we sought to explain this observation by examining in detail the habitat preferences of seropositive rodents (Armién B, unpublished data).[26]

In spite of multiple hantaviruses in Panama, human infection appears to be exclusively caused by Choclo virus. First, in all acute-phase human sera from HCPS patients tested to date for viral genome by RT-PCR, only Choclo virus sequences have been found (Pascale JM, unpublished data). Second, all positive serum samples from persons without a history of HCPS contained Choclo virus–neutralizing activity when tested for hantavirus antibody by neutralization inhibition assays (Koster F, unpublished data). Although we can not rule out human infection with Calabazo virus transmitted from its *Z. brevicauda* host, for the purposes of this study, the only rodent of medical interest is *O. fulvescens*.

The rodent and human seroprevalence data used two assays, an enzyme-linked immunosorbent assay and a strip immunoblot. These binding assays have shown a concordance of 98.0% in human samples from Panama (Pascale JM and Quiroz E, unpublished data).[26] The enzyme-linked immunosorbent assay and the strip immunoblot used Sin Nombre virus nucleocapsid antigen, which is cross-reactive with antibodies to all known sigmodontine-borne hantaviruses in the Americas.[21] However, these methods do not identify the viral strain. Preliminary sequencing of 600 basepairs by RT-PCR amplimers from tissue RNA from seropositive *S. hirsutus* specimens indicates that these viruses are not closely related, but additional characterization is required.

Earlier comparisons of small-mammal assemblages showed the highest small-mammal diversity in natural ecosystems and the highest abundance in human-altered ecosystems.[23,43] Our data support the notion that Choclo, Calabazo and *S. hirsutus*-associated hantaviruses are concentrated on the human-dominated habitat, whereas others hantavirus such as the *Peromyscus mexicanus*- and *Reithrodontomys* spp.-associated hantavirus appeared to be restricted to the tropical upland natural forests of the extreme western region of Panama (Volcan Baru in Chiriqui Province).[24,25,43] Furthermore, *Z. brevicauda*, the host of Calabazo virus, was the only reservoir species consistently present and the most abundant reservoir in agroecosystems from the extreme west to the extreme east of the Isthmus of Panama (Armién B, unpublished data). In central-western Panama, *O. fulvescens* and *Z. brevicauda* were consistently found in the MPS but were uncommon in TPS (Table 1). In contrast, *S. hirsutus* was more common and more often seropositive in the TPS than in the MPS.

Our data is consistent with the hypothesis that increased rodent density and competition is a cause of increased seroprevalence. For *O. fulvescens* and *Z. brevicauda*, but not *S. hirsutus,* antibody prevalence was associated with sex, wounding, and body weight, a surrogate for age, agreeing with multiple studies on rodent reservoirs of American hantavirus.[18,20,39,40,44,45] Although aggressive encounters among adult males may

TABLE 2
Distribution of *Oligoryzomys fulvescens, Zygodontomys brevicauda*, and *Sigmodon hirsutus* tested for antibody against hantaviruses by sex, weight, and presence of wounds in agroecosystems in central-western Panama, 2002–2006*

	O. fulvescens			Z. brevicauda			S. hirsutus		
Characteristic	% (IgG+/n)	OR (95% CI)	P	% (IgG+/n)	OR, (95% CI)	P	% (IgG+/n)	OR (95% CI)	P
Sex									
Male	29.3 (48/164)	2.18 (1.16–4.18)	0.0107	11.9 (111/932)	5.40 (3.18–9.69)	< 0.0001	0.5 (1/213)	0.19 (0.004–1.69)	0.1143
Female	16.0 (19/119)	1		2.4 (17/696)	1		2.5 (5/203)	1	
Weight									
Juvenile-subadult	13.4 (16/119)	1		1.2 (9/753)	1		0.7 (1/152)	1	
Adult	31.1 (51/164)	2.90 (1.51–5.79)	0.0006	13.6 (119/875)	13.01 (6.55–29.34)	< 0.0001	4.6 (5/264)	2.91 (0.32–138.77)	0.4224
Wound									
Yes	39.5 (30/76)	3.00 (1.60–5.56)	0.0003	13.0 (44/338)	2.15 (1.42–3.20)	0.0002	2.2 (2/90)	1.21 (0.12–6.93)	0.6850
No	17.9 (37/207)	1		6.5 (84/1,290)	1		1.2 (4/326)	1	
Male									
Yes	48.1 (25/52)	3.58 (1.65–7.75)	0.0005	19.6 (38/194)	2.22 (1.40–3.47)	0.0004	0.0 (0/43)	–	1.0000
No	20.5 (23/112)	1		9.9 (73/738)	1		0.6 (1/170)	1	
Female									
Yes	20.8 (5/24)	1.52 (0.38–5.20)	0.5337	4.2 (6/144)	2.02 (0.60–6.08)	0.2266	4.3 (2/47)	2.27 (0.18–20.33)	0.3279
No	14.7 (14/95)	1		2.0 (11/552)	1		1.9 (3/156)	1	

* Fisher's exact test was used to estimate the *P* value. % = percentage of individuals with antibodies against hantavirus; IgG+ = no. of rodents that were antibody reactive to hantavirus; n = no. of mice for each category.

account for much of the transmission within rodent populations,[44–47] other aspects such as social behaviors and habitat features have also been proposed as additional factors influencing transmission.[7,16,42,45]

Risk to humans is a function of frequency of seropositivity and relative abundance in habitats frequented by persons. Crops within 40 meters of a residence contained the highest percentage of seropositive *O. fulvescens* compared with pastures and other vegetation types in paradomestic environments (Figure 2). However, because of increased relative abundance, greater numbers of seropositive *O. fulvescens* were captured in ornamental gardens. Seropositive rice rats (*O. fulvescens*) were more common in the traditional (non-mechanized) mixed cultivation of corn and vegetables (42.9%, 12 of 28) than in the mechanized monocultures of rice (17.4%, 4 of 23) (Armién A, unpublished data). However, crops within 40 meters of residences may have special significance because the nocturnal foraging distance for these rodents was 30–40 meters as determined by radiotelemetry in one of our intensively surveyed sites (Armién B, unpublished data). Thus, during the post-harvest dry season when seed availability was reduced in the field, rodent foraging near residences would not require long-distance travel to reach intra-habitation food. Long-term data from mark-recapture studies may help clarify the relationship between antibody prevalence, rodent community structure, density, and home range for paradomestic environments.[16,19,20,37,38,41,45,48]

The physical relationship between crops and ornamental gardens near human residences may have public health implications. Thus, one potential intervention may be relocating crops away from residences, locating short grass near residences, and identifying the plants in ornamental gardens that attract *O. fulvescens*. Future studies will examine food storage and preparation in and near residences. In a future contribution, detailed analyses of serial assessments of human and rodent seroprevalence by site, habitat, season, and year will clarify the dynamic relationship between human and rodent seroconversions in the same communities.[41,42]

Note: Supplemental tables 3 and 4 and supplemental figure 5 appear online at www.ajtmh.org.

Authors' addresses: Aníbal G. Armién, Department of Population Medicine, College of Veterinary Medicine, University of Minnesota, Saint Paul, MN 55108, E-mail: armie001@umn.edu. Blas Armién, Juan M. Pascale, Publio Gonzalez, Manuel de la Cruz, Yamizel Zaldivar, and Yaxelis Mendoza, Instituto Conmemorativo Gorgas de Estudios de la Salud, Avenida Justo Arosemena, Apartado 6991, Zona 5, Panama, E-mail: barmien@gorgas.gob.pa. Mario Avila, Instituto Conmemorativo Gorgas de Estudios de la Salud, Avenida Justo Arosemena, Apartado 6991, Zona 5, Panama and Ministry of Health, Herrera Province, Panama. Frederick Koster, Lovelace Respiratory Research Institute, Albuquerque, NM 87108. Fernando Gracia, Hospital Santo Tomas, Panama City, Panama. Brian Hjelle, SOM Pathology Department, 08 4640, University of New Mexico Health Sciences Center, Albuquerque, NM 87131-0001. Sang-Joon Lee, Department of Internal Medicine, MSC 10 555, University of New Mexico Health Sciences Center, Albuquerque, NM 87131-0001. Jorge Salazar-Bravo, Center for Epidemiology and Zoonoses, Department of Biological Sciences, Texas Tech University, Lubbock, TX 79409.

Reprint requests: Blas Armién, Instituto Conmemorativo Gorgas de Estudios de la Salud, Avenida Justo Arosemena, Apartado 6991, Zona 5, Panama, E-mail: barmien@gorgas.gob.pa.

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Table 3. Distribution of rodents captured by species in agroecosystems in central-western Panama, 2002—2006. Numbers are percent of total captures attributed to each species; numbers of captures given in parentheses.

Species	Agroecosystems		Total (N)
	Mixed productive system	Traditional productive system	
Heteromyidae			
Heteromys desmarestianus	0.0 (1)	- (-)	1
Liomys adspersus	6.5 (188)	38.6 (214)	402
Muridae			
Mus musculus	1.0 (28)	- (-)	28
Rattus rattus	0.2 (7)	0.5 (3)	10
Echimyidae			
Proechimys semispinosus	- (-)	0.4 (2)	2
Cricetidae			
Nyctomys sumichrasti	0.0 (1)	- (-)	1
Oligoryzomys fulvescens	10.9 (314)	1.1 (6)	320
Oryzomys bolivaris	0.0 (1)	0.2 (1)	2
Oecomys trinitatis	0.1 (2)	- (-)	2
Oryzomys couesi	0.1 (3)	0.5 (3)	6
Oryzomys talamancae	0.1 (2)	0.4 (2)	4
Reithrodontomys darienensis	0.0 (1)	- (-)	1
Sigmodon hirsutus	15.6 (451)	51.3 (284)	735
Zygodontomys brevicauda	65.5 (1893)	7.0 (39)	1932
Total individuals	2892	554	3446
Species	13	9	14
Effective trap nights	61405	14528	75933
Trap success (Individuals)	4.7	3.8	4.5
Trap success (species)	0.02	0.06	0.02

Traps success (%)

Table 4. Percentage of antibodies against to hantavirus nucleoprotein and relative abundance of rodents capture for *Oligoryzomys fulvescens* (*Of*), *Zygodontomys brevicauda* (*Zb*) and *Sigmodon hirsutus* (*Sh*) by vegetation type in peridomestic habitat in mixed productive system in Panama 2002—2006.

Vegetation	*Oligoryzomys fulvescens*[1]		*Zygodontomys brevicauda*[2]		*Sigmodon hirsutus*[3]	
	P; 95% CI (n)	RA	P; 95% CI (n)	RA	P; 95% CI (n)	RA
Secondary vegetation[4]	28,9; 17,0-44,8 (38)	0.33	12,0; 8,5-16,7 (241)	2.07	5,6; 1,5-13,6 (72)	0.63
Pasture[5]	15,6; 6,5,-29,5 (45)	0.35	7,7; 5,6-10,4 (517)	4.25	- (112)	0.90
Crops[6]	32,2; 22,6-43,1 (87)	0.35	6,5; 4,7-8,8 (600)	3.11	0,6; 0,0-3,5 (157)	0.72
Total	27,1; 20,9-34,2(170)	0.35	8,0; 6,6-9,5 (1358)	3.16	1,5; 0,5-3,4 (341)	0.75

P = %; 95% Confidence Interval; n=number of mice.

RA= Relative abundance (individuals/100 traps night)

Fisher exact test were used to estimate the p-value.

[1]Secondary vegetation vs. Pasture P = 0.1838, [Odds Ratio (OR) = 2.21, 95% CI 0.67-7.60]; Pasture vs. Crops P = 0.0601, (OR=0.39, 95% CI 0.13-1.03) and Secondary vegetation vs. Crops P = 0.8347, (OR=0.86, 95% CI 0.33-2.11)

[2]Secondary vegetation vs. Pasture P = 0.0588, (OR=1.63, 95% CI 0.95-2.78); Pasture vs. Crops P = 0.4828, (OR=1.21, 95% CI 0.74-1.96) and Secondary vegetation vs. Crops P = 0.0113, (OR=1.97, 95% CI 1.14-3.35).

[3]Secondary vegetation vs. Pasture P = 0.0223; Pasture vs. Crops P > 0.9999 and Secondary vegetation vs. Crops P = 0.0349 (OR=9.18, 95% CI 0.87-454.72).

[4]*Of vs. Zb* P = 0.0109, (OR=2.98, 95% CI 1.19-7.00); *Of vs. Sh* P = 0.0022, (OR=6.92, 95% CI 1.81-31.82) and *Zb vs. Sh* P = 0.1309, (OR=2.32, 95% CI 0.77-9.41).

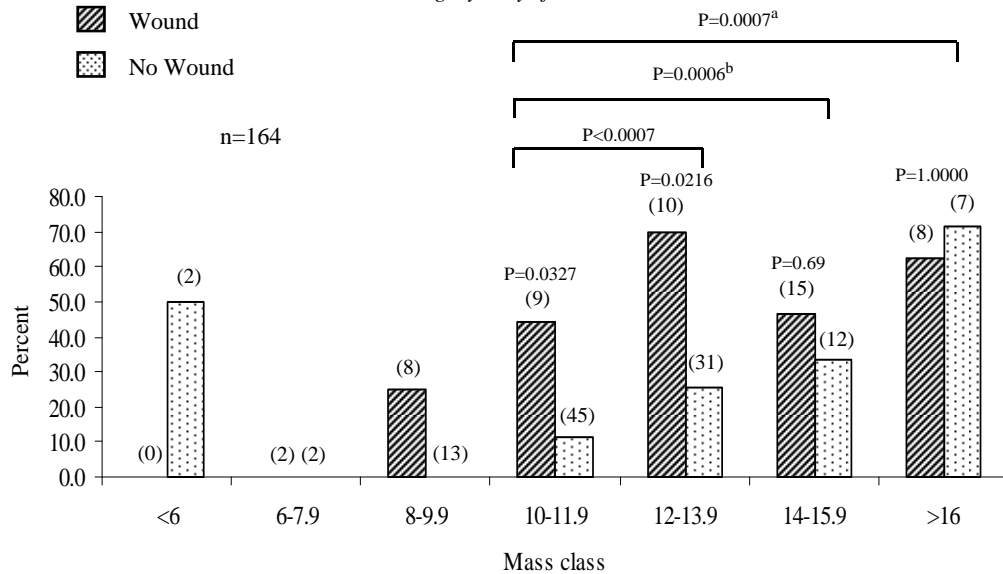[5]*Of vs. Zb* P = 0.0866, (OR=2.20, 95% CI 0.78-5.41); *Of vs. Sh* P = 0.0001 and *Zb vs. Sh* P = 0.0004.

[6]*Of vs. Zb* P < 0.0001, (OR=6.83, 95% CI 3.74-12.27); *Of vs. Sh* P < 0.0001, (OR=74.03, 95% CI 11.52-3045.85) and *Zb vs. Sh* P = 0.0012, (OR=10.84, 95% CI 1.80-441.97).
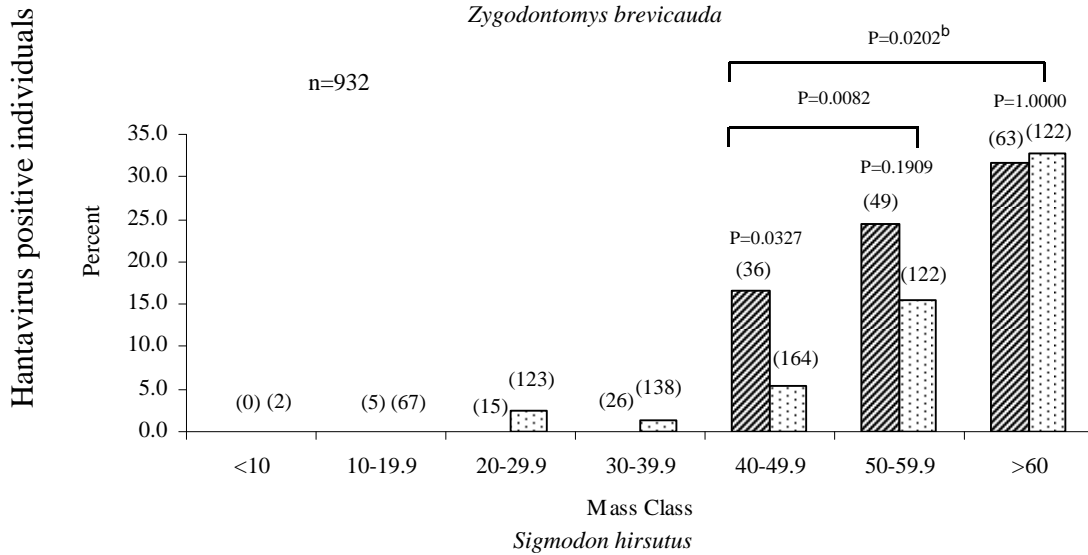
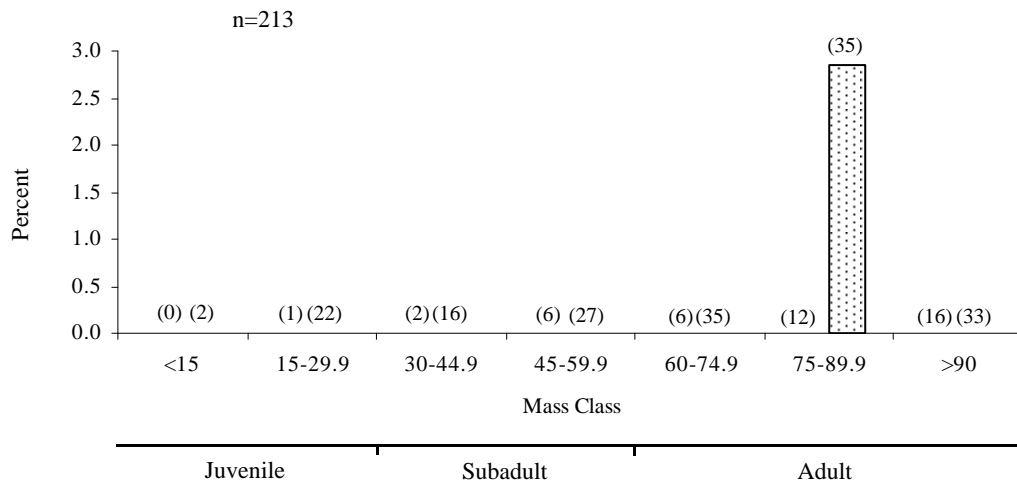[1-6]The cut-off value for significance level is 0.0167 using Bonferroni correction.

Male

Oligoryzomys fulvescens

P=0.0007[a]

P=0.0006[b]

P<0.0007

n=164

Legend:
- Wound (hatched)
- No Wound (dotted)

Percent (y-axis): 0.0, 10.0, 20.0, 30.0, 40.0, 50.0, 60.0, 70.0, 80.0

Mass class (x-axis): <6, 6-7.9, 8-9.9, 10-11.9, 12-13.9, 14-15.9, >16

P-values and counts:
- <6: (0), (2)
- 6-7.9: (2), (2)
- 8-9.9: (8), (13)
- 10-11.9: P=0.0327, (9), (45)
- 12-13.9: P=0.0216, (10), (31)
- 14-15.9: P=0.69, (15), (12)
- >16: P=1.0000, (8), (7)

Zygodontomys brevicauda

P=0.0202[b]

P=0.0082

P=1.0000

n=932

Percent (y-axis): 0.0, 5.0, 10.0, 15.0, 20.0, 25.0, 30.0, 35.0

Mass Class (x-axis): <10, 10-19.9, 20-29.9, 30-39.9, 40-49.9, 50-59.9, >60

Counts and p-values:
- <10: (0), (2)
- 10-19.9: (5), (67)
- 20-29.9: (15), (123)
- 30-39.9: (26), (138)
- 40-49.9: P=0.0327, (36), (164)
- 50-59.9: P=0.1909, (49), (122)
- >60: (63), (122)

Sigmodon hirsutus

n=213

Percent (y-axis): 0.0, 0.5, 1.0, 1.5, 2.0, 2.5, 3.0

Mass Class (x-axis): <15, 15-29.9, 30-44.9, 45-59.9, 60-74.9, 75-89.9, >90

Counts:
- <15: (0), (2)
- 15-29.9: (1), (22)
- 30-44.9: (2), (16)
- 45-59.9: (6), (27)
- 60-74.9: (6), (35)
- 75-89.9: (12), (35)
- >90: (16), (33)

Age groups: Juvenile | Subadult | Adult

Hantavirus positive individuals (y-axis label)

Fisher exact test were used to estimate the p-value.
[a]The cut-off value for significance level is 0.0125 using Bonferroni.
[b]The cut-off value for significance level is 0.0167 using Bonferroni.
Mass class (gram)