

BLACK CREEK CANAL VIRUS INFECTION IN *SIGMODON HISPIDUS* IN SOUTHERN FLORIDA

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Abstract. A total of 1,500 small mammals were collected and tested for antibodies cross-reactive to Sin Nombre virus (*Hantavirus*: Bunyaviridae) at 89 sites in a 1,600 km² study area of southern Florida. More than 95% of the 123 seropositive animals were cotton rats (*Sigmodon hispidus*), suggesting infection by Black Creek Canal Virus, although seroreactive *Rattus rattus* (5 of 294) and *Peromyscus gossypinus* (1 of 39) also were captured. Crude seroprevalence in *S. hispidus* was 11%. Seroprevalence increased with body size and was more common in male (18%; n = 451) than in female (6%; n = 593) cotton rats. Infection within *S. hispidus* populations was widespread throughout the study area. Prevalence ranged from 0% to 60% at sites where more than five cotton rats were sampled but was not only a function of sample size. Sites with seropositive cotton rats were geographically clustered compared with sites with no seropositive cotton rats. Clustering was not due to the spatial distribution of sites with few animals, season of collection, or sex bias of animals captured at these sites. However, sites with no seropositive animals had an excess of animals in the intermediate size class (60–99 g) and a deficit of the largest and smallest animals. These data suggest that population structure within the habitat mosaic may play a significant role in the spatial distribution of hantavirus infection in local populations of reservoir species.

In the summer of 1993, the emergence of a previously unrecognized syndrome of acute respiratory distress, associated with high mortality,¹ led to the identification of a previously unrecognized hantavirus (Family Bunyaviridae),² the implication of a Sigmodontine rodent, *Peromyscus maniculatus*, as the reservoir,³ and the clinical and pathologic characterization of hantavirus pulmonary syndrome (HPS).⁴ Subsequently, several cases of HPS were identified in regions outside the geographic range of *P. maniculatus*.^{5,6} Based on previous evidence that most hantaviruses tended to have a single rodent reservoir it was anticipated that other pathogenic hantaviruses were responsible for these cases, and that other rodents served as their reservoirs.

Early in 1994, a case of HPS was identified in southern Florida and serologic studies showed reactivity between the patient's sera and recombinant antigens developed against Sin Nombre virus (SNV) from *P. maniculatus*.⁷ Preliminary surveys of the rodent fauna in the area showed a high prevalence of reactivity to SNV in cotton rats (*Sigmodon hispidus*, Say and Ord) with low prevalences in the remaining species. Subsequently, the isolation and characterization of a hantavirus from two of these cotton rats was described. Partial sequence analysis showed the virus, named Black Creek Canal virus (BCCV), to be a unique member of the genus *Hantavirus*.⁸

In studies of other reservoirs,^{9,10} hantavirus infection appeared to be transmitted horizontally so that the prevalence of infection increased with age in the reservoir animals. In addition, infection was geographically widespread, subsuming most of the reservoir's distribution. Some studies noted that infection occurred with approximately equal frequency in both sexes,⁹ while in other reservoir species infection predominated in males.¹⁰ The purpose of this project was to characterize BCCV infection within the rodent fauna in southern Florida, especially its putative reservoir *S. hispidus*, in a more extensive manner than was possible during the

preliminary surveys. Particular attention was focused on the spatial distribution of infection in local reservoir populations.

METHODS

Trapping of small mammals was undertaken from August to December 1994 at 110 sites throughout Dade County in southern Florida. Sampling methods, described elsewhere in more detail,⁸ consisted of lines of 48 Sherman live traps set in grassy, semi-wooded and residential areas throughout a region of approximately 1,600 km². Traps were baited with a mixture of bird seed and peanut butter and set for three consecutive nights, yielding an equal sampling effort of 144 trap-nights at each site. The study area was bounded on the east by Biscayne Bay, on the west by SW 217th Avenue, on the north by Sunset Drive, and on the south by Palm Drive. Results from 89 sites where at least one *S. hispidus* was captured are described.

Live-trapped animals were brought to a central processing location where they were anesthetized, identified to species, standard external measurements were recorded, blood was collected, and the animals were killed.¹¹ During trapping and processing, recommended procedures were followed to reduce the risk of exposure for personnel.¹² Collected sera were either sent to the Centers for Disease Control and Prevention (Atlanta, GA) or the Florida State Health Laboratory (Jacksonville, FL) for testing for antibodies to hantavirus. For consistency with the preliminary studies, SNV antigen was used as the test antigen in an ELISA format. Early studies showed there was relatively little loss in sensitivity, in cotton rats, using SNV antigen (16 of 90 positive), rather than BCCV antigen (17 of 90 positive), and that all cotton rats with amplifiable viral nucleic acids were infected with BCCV.⁸ Details of serologic testing were described previously.⁸ Briefly, an *Escherichia coli* recombinant SNV nucleocapsid antigen was coated on an ELISA plate. Negative

TABLE 1
Species composition, numbers tested, and numbers seropositive by ELISA to Sin Nombre Virus antigen

Species	Number tested	Number positive	Seroprevalence (%)
<i>Sigmodon hispidus</i>	1,041	117	11.2
<i>Oryzomys palustris</i>	22	0	0.0
<i>Peromyscus gossypinus</i>	39	1	2.6
<i>Rattus rattus</i>	294	5	1.7
<i>Rattus norvegicus</i>	40	0	0.0
<i>Mus musculus</i>	64	0	0.0
Total	1,500	123	8.2

control wells used the *E. coli* without SNV nucleocapsid. Whole blood was diluted 1:100 in 5% skim milk with phosphate-buffered saline (PBS)-0.05% Tween and allowed to react with the antigen-coated wells. Bound IgG was detected with a mixture of goat anti-rat and goat anti-*Peromyscus* IgG conjugated to horseradish peroxidase. Optical densities (ODs) at 410 nm were recorded and the ODs from the negative control wells were subtracted from the ODs of the SNV recombinant antigen wells. In this paper a serologic response to SNV antigen was assumed to be caused by BCCV since *S. hispidus* has been implicated as the primary or sole reservoir to BCCV and no other hantavirus has been found among individuals of this species in this area.

Seroprevalence was calculated as the number of seropositive animals divided by the numbers of animals tested for selected strata of the data. Prevalence was examined for male and female rats separately, and the population was divided into mass classes, as a surrogate of age. The five mass classes were < 60 g, 60–99 g, 100–149 g, 150–199 g and ≥ 200 g. Cotton rats < 60 g are generally sexually immature while animals ≥ 100 g are usually reproductively mature.¹³ Differences in the seroprevalence by mass class and sex were tested by log-linear models using counts of seropositive and seronegative individuals.

The geographic distribution of sites with infected cotton rats was examined by the method of Cuzick and Edwards¹⁴ for sites with \geq five sampled cotton rats. The T_k statistic, a measure of spatial aggregation, was used in this study to assess whether sites with infected cotton rats were spatially clustered when compared with sites that did not have infected cotton rats. The correction of Simes¹⁵ was used for multiple tests of nearest neighbors. Sites with five collected *S. hispidus* were included because the proportion of these sites with infected rats (50%) was not different from sites where more rats were sampled, and sites with small numbers of collected cotton rats were not themselves spatially clustered. Tests for differences in proportions were used to determine if epizootiologic characteristics and season of collection contributed to spatial clustering of sites with infected cotton rats.

RESULTS

A total of 1,500 small mammals was trapped and tested during the survey (Table 1). *Sigmodon hispidus* was the predominant species captured (69.4%). This was, in part, influenced by the selection of the habitats associated with trapping sites, but even outside urban settings preliminary sur-

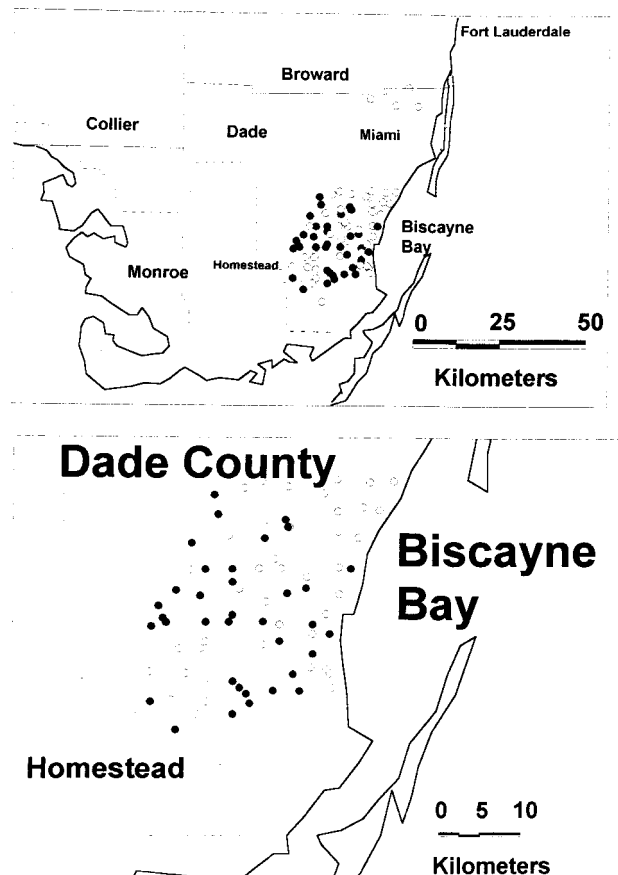


FIGURE 1. Map of collection sites of *Sigmodon hispidus* in southern Florida. The heavy solid line indicates the coastline. Thin solid lines are county boundaries (Broward, Collier, Dade, and Monroe). The approximate locations of three cities (Fort Lauderdale, Miami, and Homestead) are indicated by names. The dotted line shows the approximate northern boundary of Everglades National Park. Collecting sites with seropositive *S. hispidus* (solid circles) and sites with no seropositive *S. hispidus* (open circles) are shown for the entire study area (top) and for the study sites in the main body of the collecting area (bottom).

veys showed that cotton rats predominated in the local fauna.⁸ *Sigmodon hispidus* (Table 1) had the highest seroprevalence to SNV antigen (11.2%) of any of the species tested. A single *P. gossypinus* (1 of 39) and five *Rattus rattus* (5 of 294) also tested positive for SNV antigen.

Sigmodon hispidus were caught at 89 of 110 sites that were sampled. The mean number of rats captured per site, where they occurred, was 11.7 (range = 1–51) and at least five *S. hispidus* were caught 65.1% (58 of 89) of these sites. Seropositive *S. hispidus* were trapped at 46.1% of the 89 sites, which represented a variety of land use types including agricultural, residential, recreational, and industrial sites (Florida Department of Health and Rehabilitative Services, unpublished data). Infected *S. hispidus* were found at 35 (60.3%) of 58 sites with five or more sampled cotton rats. The average seroprevalence of *S. hispidus* at these sites was 20.7%. Sites with seropositive *S. hispidus* occurred throughout the study area, but tended to be more common in the southern and western regions (Figure 1). Overall, sites with infected *S. hispidus* were geographically clustered. Except for sites immediately adjacent to sites with infected *S. his-*

TABLE 2

Spatial aggregation of sampling sites with seropositive *Sigmodon hispidus* to Sin Nombre virus*

K	T _k	P†
1	22	0.352
2	50	0.022
3	73	0.020
4	94	0.041
5	117	0.031
6	143	0.009
7	162	0.028
8	181	0.060
9	202	0.079
10	219	0.172

* The test of Cuzick and Edwards was performed using sites where at least five cotton rats were tested. Sites with at least one seropositive animal served as case sites and sites where all were negative served as control sites. K represents the k-th order nearest site. T_k is the test statistic that measures the number of times a site with infected cotton rats was the k-th order neighbor of another site with infected rats, and P is the level of significance. A P < 0.05 indicates that there was a statistically significant clustering of case sites that were k-th neighbors.

† Overall significance P = 0.047.

pidus, the next seven nearest collections also were more likely to have infected *S. hispidus* than expected by chance (T₂₋₇ < 0.05; Simes correction of Bonferroni method P = 0.047; Table 2). At greater distances, the distribution of sites with infected and uninfected cotton rats were randomly distributed with respect to one another.

Finding seropositive *S. hispidus* was not simply a reflection of trap success. At eight (34.8%) of 23 sites where ≥ 19 animals were tested, no seropositive *S. hispidus* were captured. There also was no significant difference in the proportion of negative and positive sites sampled throughout the three seasons of trapping ($\chi^2 = 0.01$, P = 0.997, degrees of freedom [df] = 2). Sites with infected *S. hispidus* had a slightly higher proportion of male rats than negative sites (44.7% versus 40.7%) but the difference was not statistically significant ($\chi^2 = 1.48$, P = 0.224). However, there was a significant difference in the size structures of the population of males collected at uninfected or infected sites ($\chi^2 = 18.73$, P < 0.001, df = 4). Sites with no positive *S. hispidus* had fewer than expected small (< 60 g) male rats (15 observed, 23.7 expected), fewer of the largest (≥ 200 g) male *S. hispidus* (0 observed, 5.1 expected), and more of the males reaching sexual maturity (60–99 g) than expected (35 observed, 25.4 expected). The size structures of the female populations at infected and uninfected sites were not significantly different ($\chi^2 = 7.92$, P = 0.094), although there also tended to be an excess of females reaching sexual maturity (60–99 g) at the uninfected sites (63 observed, 52.5 expected).

Seroprevalence increased with increasing body mass (Figure 2) for both sexes. In juvenile (< 60 g) and young adult (60–99 g) *S. hispidus*, seroprevalence was approximately 2–4% and did not differ between males and females. In larger *S. hispidus*, seroprevalence increased with body mass (Figure 2) and increased more rapidly for males than females. The log linear model providing the best fit to the data ($\chi^2 = 6.43$, P = 0.09, df = 3) indicated a statistically significant association between sex and seropositivity, a significant increase in the proportion of seropositive animals with size, and a significant increase in the proportion of large rats that were males. In the largest mass class (≥ 200 g), when 77.3%

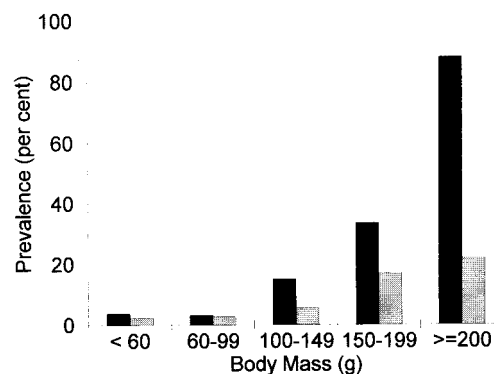


FIGURE 2. Size-associated seroprevalence in male (black bars) and female (gray bars) *Sigmodon hispidus*. Prevalence increased with body mass and increased more rapidly in male than in female *S. hispidus*.

of the animals collected were male, nearly all male rats were seropositive (88.2%) while only 20.0% of females of this size were seropositive. A more detailed (< 30 g versus 31–59 g) examination of seroprevalence in the smallest mass class (< 60 g) showed a marked decrease in seroprevalence from the smallest to the larger mass (9.1%; n = 55 versus 2.0%; n = 101) before the onset of reproduction.

DISCUSSION

This study supports a growing number of reports characterizing the epizootiology of hantavirus infections in natural reservoir hosts. As with previous studies, seroprevalence to hantavirus tended to be common only in a restricted number of sampled species (Table 1).^{3,10,16,17} For example, a recent survey of more than 3,000 small mammals, representing 69 different species, found antibodies to SNV in only nine species and in four of these antibody was found in only a single individual.¹⁰ To date, hantaviruses appear to have rodents of the family Muridae as their primary hosts.

As with other Sigmodontine reservoirs, seroprevalence in *S. hispidus* increases with size of the animal and is more common in males than females. The consequences of this pattern is that the prevalence of infection is affected by the size structures and sex ratios of local populations, which is influenced by population dynamics of the rodents. In addition to supporting the general picture of hantavirus epizootiology, this study demonstrates a mesoscale geographic clustering of hantavirus infection and establishes an association between population structure and the geographic distribution of hantavirus infection in the reservoir species.

Although we used heterologous antigen to detect antibody to BCCV, the excellent cross-reactivity between SNV and BCCV suggests that few seropositive *S. hispidus* were not identified. Conversely, interpreting positive serological results as indicative of BCCV infection is supported by the polymerase chain reaction amplification of viral nucleic acids and the previous isolation of BCCV from seropositive *S. hispidus* from these sites,⁸ as well as the relative paucity of seroreactive specimens from other species (Table 1).

The relationship between body size and seroprevalence (Figure 2) implies that collected samples with predominantly larger (older) animals are more likely to have infected in-

dividuals than samples that represent predominantly smaller (younger) animals.^{3,10,18} The somewhat higher seroprevalence observed in the smallest body size class is thought to reflect the presence of maternal IgG antibody in offspring that is catabolized, resulting in a decreasing seroprevalence from the smallest to the larger juvenile mass classes, until infection at a later age produces increased seroprevalence.^{16,19–21} The decrease in seroprevalence among *S. hispidus* from 9% to 2% in the two subadult size classes mirrors the patterns noted for SNV in *P. maniculatus* in which prevalence decreased from 14% to 1% in the smallest mass classes before increasing among adult mice.¹⁰ The strong skew towards seropositive males in older *S. hispidus* also is consistent with previous reports from Sigmodontine rodents.^{3,10} The higher rates of seroprevalence in older male rodents has been hypothesized to be caused by aggressive intrasexual interactions among adult male Sigmodontine rodents¹⁰ and aggression among adult rodents is reported common.^{16,22} However, in the present study, no information was recorded on the presence or frequency of biting that would allow us to evaluate this hypothesis for the maintenance of BCCV.

The systematic sampling of this study showed that a large proportion of sites within the study area yielded no infected *S. hispidus*, even though the species was common. Earlier studies of *P. maniculatus* sampled during the HPS outbreak investigation of 1993 also indicated some sites had no captures of seropositive mice,³ an observation supported by smaller surveys in Kansas.¹⁸ A large serosurvey throughout the southwestern United States also found no seropositive deer mice at 20 of 41 sampling sites where the species was collected, although positive mice occurred throughout the geographic region.¹⁰

Various hypotheses can be evaluated to explain sites without seropositive *S. hispidus*. One possible explanation could be that these areas merely reflected insufficient sampling. Although this may explain some of the sites where relatively few animals were sampled, it does not explain the absence of seropositive animals at many of the localities. Even at the 23 sites where ≥ 19 *S. hispidus* were captured, nearly 35% of those locations yielded no seropositive animals, a value not significantly different from the 40% of seronegative sampling sites when only ≥ 5 animals were tested. Another explanation for finding uninfected sites was the timing of collections because not all sites could be sampled within a single sampling interval. However, we think this is unlikely because there were no seasonal pattern in the proportion of seronegative sites that were sampled.

In the absence of methodologic reasons for this pattern, alternative explanations for sites without infected animals involve the interplay of viral transmission and reservoir population dynamics as they affect the persistence of hantavirus in local reservoir populations. The significant effects of sex, body size, and their interaction on seroprevalence suggests that differences in sex ratios among sites could influence local seroprevalence rates. However, we found no significant difference in the sex ratios of populations from sites without infected animals when compared to sites with infected animals and therefore conclude that differences in sex ratio were not responsible for the occurrence of uninfected sites.

The major feature that distinguished sites without seropositive *S. hispidus* was the higher than expected number of

subadults captured at these locations, and, especially among males, the paucity of the largest and smallest size classes of animals. Thus, these sites may reflect a commonly reported phenomenon related to dispersal of maturing rodents. As juvenile rodents mature, they typically disperse from their natal burrows and establish their own territories or home ranges.²³ Aggressive interactions with resident animals are thought to drive dispersal activity to new sites.^{22–24} Dispersal sinks for *S. hispidus* then represent areas where there are a disproportionate number of dispersing subadults (60–99 g). This is the size class with the lowest seroprevalence and if BCCV, like other hantaviruses, is horizontally transmitted, then these subadults would tend to be uninfected when they reached these sites.²⁵

The geographic clustering of sites with infected *S. hispidus* (Table 2) may reflect larger, more contiguous, patches of suitable habitats to the west and south of the Miami region because most of the human development occurs adjacent to the Atlantic coast where infection can be more easily maintained and transmitted by local movements of individuals. These patterns of focality of infection suggest that the presence of a reservoir species is necessary but not sufficient for hantaviral disease outbreaks and it may be possible to characterize habitats that support sufficient populations of animals for the persistence of hantaviruses, based on landscape patterns, by linking remotely sensed data to infection patterns in local populations.

The results of this and other recent studies point to the need for careful data collection, identification, and documentation of the characteristics of locally sampled populations of hantavirus reservoirs. The apparent epizootiology of the viruses is influenced by the species collected, the size structure and sex ratio of the sample collected, as well as the habitat in which the sampling is conducted. The success in understanding patterns of hantavirus maintenance and transmission in various species across studies will be limited unless researchers consider these potentially confounding factors that affect the patterns of infection.

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REFERENCES

1. CDC, 1993. Outbreak of acute illness—southwestern United States. *MMWR Morb Mortal Wkly Rep* 42: 421–424.
2. Nichol ST, Spiropoulou CF, Morzunov S, Rollin PE, Ksiazek TG, Feldmann H, Sanchez A, Childs J, Zaki S, Peters CJ, 1993. Genetic identification of a hantavirus associated with an outbreak of acute respiratory illness. *Science* 262: 914–917.
3. Childs JE, Ksiazek TG, Spiropoulou CF, Krebs JW, Morzunov S, Maupin GO, Rollin PE, Sarisky J, Ensore RE, 1994. Serologic and genetic identification of *Peromyscus maniculatus* as the primary rodent reservoir for a new hantavirus in the southwestern United States. *J Infect Dis* 169: 1271–1280.
4. Zaki SR, Greer PW, Coffield LM, Goldsmith CS, Nolte KB, Foucar K, Feddersen RM, Zumwalt RE, Miller GL, Khan AS, Rollin PE, Ksiazek TG, Nichol ST, Mahy BWJ, Peters CJ, 1995. Hantavirus pulmonary syndrome: pathogenesis of an emerging infectious disease. *Am J Pathol* 146: 552–579.
5. CDC, 1994. Newly identified hantavirus—Florida, 1994. *MMWR Morb Mortal Wkly Rep* 43: 99 and 105.
6. Khan AS, Spiropoulou CF, Morzunov S, Zaki SR, Kohn MA, Nawas SR, McFarland L, Nichol ST, 1995. Fatal illness associated with a new hantavirus in Louisiana. *J Med Virol* 46: 281–286.
7. Khan AS, Gaviria M, Rollin PE, Hlady WG, Ksiazek TG, Armstrong LR, Greenman R, Raavkov E, Kolber M, Anapol H, Sfakianaki ED, Nichol ST, Peters CJ, Khabbaz RF, 1996. Hantavirus pulmonary syndrome in Florida: association with the newly identified Black Creek Canal virus. *Am J Med* 100: 46–48.
8. Rollin PE, Ksiazek TG, Elliott LH, Ravkov EV, Martin ML, Morzunov S, Livingstone W, Monroe N, Glass G, Ruo S, Khan AS, Childs JE, Nichol ST, Peters CJ, 1995. Isolation of Black Creek Canal virus, a new hantavirus from *Sigmodon hispidus* in Florida. *J Med Virol* 46: 35–39.
9. Childs JE, Korch GW, Glass GE, LeDuc JW, Shah KV, 1987. Epizootiology of *Hantavirus* infections in Baltimore: isolation of a virus from Norway rats, and characteristics of infected rat populations. *Am J Epidemiol* 126: 55–68.
10. Mills JN, Ksiazek TG, Ellis BA, Rollin PE, Nichol ST, Yates TL, Gannon WL, Levy CE, Engelthaler DM, Davis T, Tanda DT, Frampton JW, Nichols CR, Peters CJ, Childs JE, 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. *Am J Trop Med Hyg* 56: 273–284.
11. Mills JN, Yates TL, Childs JE, Parmenter RR, Ksiazek TG, Rollin PE, Peters CJ, 1995. Guidelines for working with rodents potentially infected with hantaviruses. *J Mammal* 76: 716–722.
12. Mills JN, Childs JE, Ksiazek TG, Peters CJ, 1995. *Methods for Trapping and Sampling Small Mammals for Virologic Testing*. Atlanta, GA: Centers for Disease Control and Prevention.
13. Slade NA, Sauer JR, Glass GE, 1984. Seasonal variation in field determined growth rates of the cotton rat (*Sigmodon hispidus*). *J Mammal* 65: 263–270.
14. Cuzick J, Edwards R, 1990. Spatial clustering for inhomogeneous populations. *J R Stat Soc Ser B* 52: 73–104.
15. Simes RJ, 1986. An improved Bonferroni procedure for multiple tests of significance. *Biometrika* 73: 751–754.
16. Childs JE, Glass GE, LeDuc JW, 1991. Rodent sightings and contacts in an inner city population of Baltimore, Maryland USA. *Bull Soc Vector Ecol* 16: 245–255.
17. Otteson EW, Riolo J, Rowe JE, Nichol ST, Ksiazek TG, Rollin PE, St Jeor SC, 1996. Occurrence of hantavirus within the rodent population of northeastern California and Nevada. *Am J Trop Med Hyg* 54: 127–133.
18. Kaufman GA, Kaufman DW, McMillan BR, Brillhart DE, 1994. Prevalence of hantavirus antibodies in natural populations of deer mice in north central Kansas. *Prairie Naturalist* 26: 209–216.
19. Dohmae K, Koshimizu U, Nishimune Y, 1993. In utero and mammary transfer of hantavirus antibody from dams to infant rats. *Lab Anim Sci* 43: 557–561.
20. Childs JE, Glass GE, Korch GW, LeDuc JW, 1987. Prospective seroepidemiology of hantaviruses and population dynamics of small mammal communities of Baltimore, Maryland. *Am J Trop Med Hyg* 37: 648–662.
21. Glass GE, Childs JE, Korch GW, LeDuc JW, 1989. Comparative ecology and social interactions of Norway rats, *Rattus norvegicus*, in Baltimore, Maryland USA. *Occ Papers Mus Nat Hist Univ Kansas* 130: 1–33.
22. Lidicker, WZ Jr, Patton JL, 1987. Patterns of dispersal and genetic structure in populations of small rodents. Chepko-Sade BD, Halpin ZT, eds. *Mammalian Dispersal Patterns: The Effects of Social Structure on Population Genetics*. Chicago: University of Chicago Press, 144–161.
23. Lidicker, WZ Jr, 1975. The role of dispersal in the demography of small mammals. Golley FB, Petruszewicz K, Ryszkowski L, eds. *Small Mammals: Their Productivity and Population Dynamics*. Cambridge: Cambridge University Press, Cambridge, 103–128.
24. Glass GE, Childs JE, Korch GW, LeDuc JW, 1988. Association of intraspecific aggression and hantavirus infection in wild rats (*Rattus norvegicus*). *Epidemiol Infect* 101: 459–472.
25. Pulliam HR, BJ Danielson, 1991. Sources, sinks, and habitat selection: a landscape perspective on population dynamics. *Am Naturalist* 137: S50–S66.