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On the relationship between the environmental history and the epidemiological situation of Argentine hemorrhagic fever

Received: 21 June 2006 / Accepted: 9 February 2007 / Published online: 11 April 2007
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Abstract The aim of this work was to establish the relationship between different Argentine hemorrhagic fever (AHF) epidemiological situations found at different sites and the related large-scale environmental conditions. Large-scale environmental records (vegetation index, temperature, precipitation and elevation) were obtained from a series of monthly NOAA satellite images and global databases considered suitable for modeling climatic and other environmental determinants of large-scale biogeographical regions. The temporal variation in vegetation for cycles of winter-summer showed a greater variation in the nonendemic region than in the other two regions. On the other hand, the average of the temporal variation in precipitation in cycles of spring–autumn was more different in the historic region than in the other two regions, and land surface temperatures in cycles of spring–autumn showed differences between the epidemic region and the other two regions. We found good separation among the epidemic, historic and nonendemic sites, with the greatest difference found between epidemic and nonendemic sites. The classification of sites showed a tendency for grouping according to the epidemiological situation, but there was some variation. It seems possible to establish a

close relationship between the state of AHF incidence and the environmental history of sites suggesting the possibility of predicting epidemiological behavior using environmental conditions derived from satellite data.

Keywords Environmental variables · Satellite images · Abundance · Rodents · Argentine hemorrhagic fever

Abbreviations AHF: Argentine hemorrhagic fever · NDVI: Normalized difference vegetation index · LST: Land surface temperature · DEM: Digital elevation model · AVHRR: Advanced very-high-resolution radiometer · NOAA: National Oceanic and Atmospheric Administration · PCA: Principal component analysis · ROI: Regions of interest

Introduction

In Argentina, *Calomys musculus* (Rodentia, Muridae) is considered to be a host of Junin (JUN) virus, the etiological agent of Argentine hemorrhagic fever (AHF) (Sabattini and Maiztegui 1970). In longitudinal studies, the number of cases of AHF was correlated with changes in the density of *C. musculus* populations (Sabattini and Maiztegui 1970; Mills et al. 1991b, 1992). These studies identified the seasonal and year-to-year fluctuations in incidence and prevalence as well as the duration of infection in the hosts. AHF epidemics are highly seasonal, with the peak number of cases and peak rodent populations occurring in May when autumn crops are harvested. In years when corn mouse population densities were relatively low, the magnitude of annual AHF epidemics was also low. But in a year (1990) when corn mouse populations and numbers of infected corn mice reached extremely high levels, an unusually severe epidemic of AHF cases followed (Mills et al. 1992).

The temporal and spatial differences in reservoir abundance could lead to significant variation in risk or incidence. Several ecological processes can result in

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strong spatial patterns of risk or incidence. Here we try to understand the causes that govern the spatial pattern and rate of AHF spread. Changes in the environment may be associated with favorable weather patterns, accelerated vegetation growth, and availability of food (Mills and Childs 1998).

In other zoonoses, it has been demonstrated that population levels and the crowding of reservoirs are important factors that can affect the prevalence of density-dependent infectious disease (Pikula et al. 2002). Laboratory studies with *C. musculus* showed that transmission of Junin virus was generally horizontal, taking place among rodents in close contact to each other (Sabattini et al. 1977). Mills et al. (1992), Mills (1999), and Sabattini et al. (1977) suggest that most rodent-rodent infection could be acquired by horizontal transmission during aggressive encounters among adults defending their territories.

In AHF, increased prevalence of infection in some sites may be due to greater rodent abundance than in others. A high density for the reservoir population may contribute to horizontal transmission of Junin virus among rodents, to the maintenance of the virus in the field, and to transmission to humans. Low abundance may prevent the virus from persisting in a population (Polop et al. 2007). If the host-virus system requires a minimum rodent population density to ensure viral maintenance through rodent-to-rodent contact, the density of reservoir populations should be a key factor in the incidence of human disease. Polop et al. (2007) demonstrate differences in rodent total abundance between endemic and nonendemic sites, and different relative abundances of *C. musculus* at a geographic scale.

Although *C. musculus* is widely distributed in central and northern Argentina (Redford and Eisenberg 1992; Porcasi et al. 2005), the AHF-endemic area occupies only a limited region of the central Argentine pampa (Mills 1999) (Fig. 1). The limits of the AHF-endemic area were defined by the occurrence of the disease in humans, but infected rodents have been detected beyond that limit (Mills et al. 1991a; Enria et al. 1998). Moreover, the population of *C. musculus* appears to be continuous inside the AHF-endemic area (Maiztegui et al. 1986). However, while the prevalence of infection in reservoir populations may be very high in some sites, it may be very low or absent at nearby sites. The lack of coincidence between host distribution limits and AHF-endemic area, and the spatial variability of disease incidence in the endemic area, may be due to a combination of causes involving host genetics, geographical boundaries, local extinctions of rodents or virus subpopulations, environmental variables, and the properties of host systems that are required to support long-term maintenance of viral symbionts (Mills 1999; Polop et al. 2007).

The AHF spatial variation arises from underlying variation in the physiological and/or biological conditions that support the reservoirs. *C. musculus* prefers mainly grassy breaks in agricultural regions, and this

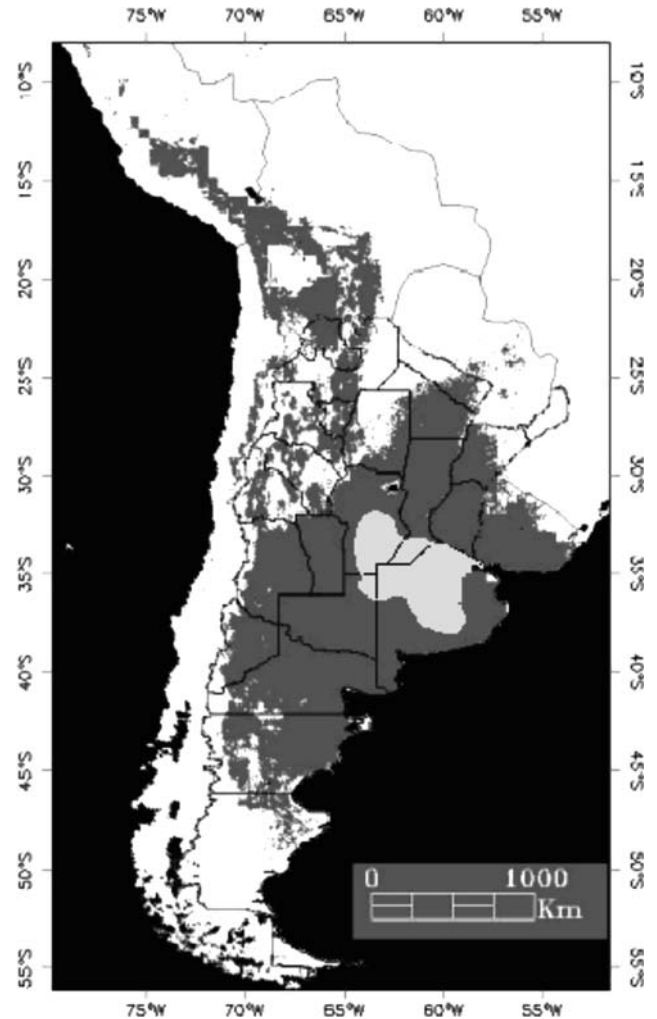


Fig. 1 Potential distribution area of *Calomys musculus* (Porcasi et al. 2005) (dark gray) and distribution area of AHF (endemic region) (light gray)

suggests that its distribution depends on weather conditions such as temperature and precipitation, which guarantee the provision of food and shelter (Busch et al. 2000). Some authors (de Villafañe et al. 1977; Polop et al. 1982; Polop et al. 2007) obtained differences in the abundance values of that species among different sites in the same season of the year, and other authors (Kravetz and Polop 1983) relate those differences to the floristic composition and the structure of landscape components. Considering that environmental variables can affect the population abundance of *Calomys* (Mills 1999; de Villafañe et al. 1992), it is valid to suppose that the observed abundance differences among the sites (Polop et al. 2007) could be associated with the environmental differences. Recognizing also the existence of a positive relation between host abundance and the spatial and temporal course of the disease (Mills 1999), environmental factors would differ among the sites with different epidemiological characterizations of AHF.

Recent advances in remote sensing of climatic and ecological features allow the identification of particular

environments that are suitable habitats for different species. Techniques that model species' requirements using environmental characteristics at sites with known occurrence represent a great advance in the production of range maps (Walker and Cocks 1991; Carpenter et al. 1993; Skov 2000; Peterson 2001). These tools introduce a new global framework for epidemiological studies by providing new variables that could improve population and epidemic modeling, as well as prevention systems for emerging infectious diseases (Cheek et al. 1998; Engelthaler et al. 1999; Beck et al. 2000; Boone et al. 2000; Glass et al. 2000; Chaput et al. 2002).

We aimed to find what factors govern the spatial pattern and the rate of AHF spread. In this context, the aim of the present study was to determine environmental differences among the sites with different characterization of the AHF incidence using remote sensing data and techniques.

Methods

Study area

The study area was the central region of Argentina, including Buenos Aires, Córdoba, Santa Fe, and La Pampa provinces. This area comprises the pampas of the Espinal and Pampeana phytogeographical provinces (Cabrera 1976). Locations of confirmed cases of AHF up to 1991 were used to define the disease endemic zone. The AHF endemic zone comprised epidemic sites characterized by disease emergence and relatively high incidence during a previous period (1987–1991), and historical sites where disease was epidemic but the incidence had diminished to fewer than 2.0/10,000 people during the 5 years. The area beyond the expanding disease front (typically to the north and west) is referred to as the nonendemic zone. The nonendemic sites did not have AHF cases reported. The sites selected to study were classified based on the onset of confirmed cases and maintenance of AHF during 1987–1991. Twenty epidemic sites, 26 historic sites and 19 nonendemic sites were considered. The location of each site and its assignment to an epidemiological condition are provided in Appendix and Fig. 2.

Environmental data

Environmental variables used for each site were monthly averages of precipitation, normalized difference vegetation index (NDVI), which is a derivative of the photosynthetically active biomass, and land surface temperature (LST), and a digital elevation model (DEM) was used. This was done with the aim of obtaining a timeless characterization of the mean, large-scale environmental conditions.

Precipitation data (Leemans and Cramer 1991) were represented as monthly mean rainfall on a latitude–

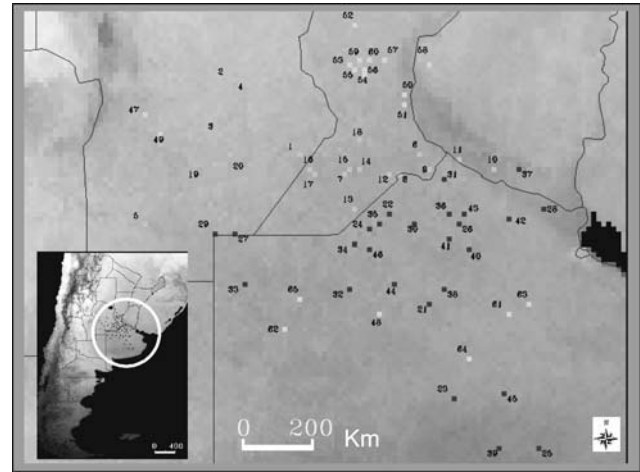


Fig. 2 Georeferenced sites with different epidemiological characterization of AHF: epidemic (*light gray*), historic (*dark gray*) and nonendemic (*white*)

longitude grid with a 30-min spatial resolution (about 50 km). The original global version of the Leemans and Cramer IIASA Climate Database is available on-line (http://www.ngdc.noaa.gov/seg/eco/cdroms/ged_iiia/go.htm). It is part of a database that contains 30 datasets, each of which is an authored work for use in global and regional biogeographical modeling. These rainfall series have been widely used in similar studies (Gilbert et al. 1999, 2001; Gorla 2001), where, in analogous way, the goal was to obtain a static representation of the large-scale mean environmental characteristics.

NDVI and LST were derived from the advanced very-high-resolution radiometer (AVHRR) onboard the National Oceanic and Atmospheric Administration's (NOAA) polar-orbiting meteorological satellites, which have a post-processing pixel size of 8×8 km. This kind of information source has also been widely used in biogeographical modeling with epidemiologic relevance (Rogers et al. 2002). NDVI and LST data are monthly averaged products derived from satellite images for the period 1982–1992. Finally, a South America DEM with 1×1 km spatial resolution from the 2.0 release version of the South America land cover characteristics database from the USGS GTOPO30 database (USGS 1998) was included in our analysis.

Environmental data were georeferenced to a latitude–longitude coordinate system and were resampled using a nearest-neighbor algorithm to adjust the pixel size to 1×1 km. Data analysis was performed using ENVI 3.5 software (System Research). Resulting data layers had $737 \times 1,037$ pixels and included South America between 13° and 56° S latitude and between 33° and 82° W longitude.

Eastman and Fulk (1993) suggest using standardized principal component analysis (PCA) to determine the predominant patterns of variance in such datasets. PCA is an attractive statistical technique to summarize information from time-series images because it decom-

poses a series into a sequence of spatial and temporal components. Typically the first component indicates the characteristic value of the variable, whereas subsequent components represent change elements of decreasing magnitude. The components may often be interpreted as related to particular environmental features or events. Applied to an image series, coarse spatial variation is typically gathered by the first PCA component. Finer-scale spatial patterns and temporal changes are captured by the second and higher order components of the PCA. Thus, PC2 of NDVI represents the temporal variation of vegetation in cycles of winter–summer; while PC3 represents cycles of spring–autumn. A similar result is seen for precipitation (Gorla 2001).

We summarized the NDVI, LST and precipitation time series using PCA analysis. The first two components of each environmental variable accounted for about 99% of the total variance in each series. Using this approach, we built a composite image of 10 layers/bands (first, second, and third PCA component of precipitation, NDVI and LST plus a single DEM layer). Each pixel of the geographic area under study was characterized by a set of these 10 variables, and all the analyses were performed on that multidimensional space.

Statistical analysis

Using ENVI 3.6 software, separate regions of interest (ROI; a collection of sample locations for an image) were constructed considering all the sites belonging to the same class of disease incidence. Each site was represented by one image pixel. Data values from the 10 layers of the composite image were extracted from the pixels in each ROI (epidemic, historic and nonendemic), and the average, maximum, minimum and standard deviation values of each environmental layer were calculated for each type of ROI. The mean values for all the pixels of each region defined a “multivariate environmental signature” that summarized the environmental characteristics of the group of pixels of each epidemiological class.

Transformed divergence separability measures or Jeffries–Matusita distances (Richards 1994) were applied to compare the regions of interest for the 10 variables. These separability values range from 0 to 2.0 and indicate how dissimilar the selected ROI pairs are. A value of 2.0 suggested 100% discrimination among classes. That means that these regions are environmentally different and distinguishable.

To determine the regions defined by the AHF epidemiological situation, a supervised classification method was applied. A classification in the context of satellite images means grouping the pixels with similar characteristics. Two sets of methods basically exist to make this grouping. One is nonsupervised, where the software alone decides which pixels are similar among them; the other method is supervised, where the researcher selects the “training sites” for each class. The supervised

process allows both for grouping pixels according to their characteristics and differentiating categories (“classes”) among them. In our case, a classical method of supervised classification, the maximum likelihood algorithm (Richards 1994), was used to assign pixels having similar characteristics to one of the three defined classes. This algorithm assumes that the variables for each class are normally distributed and calculates the probability that a given pixel belongs to a specific class, along with an established confidence measure. Thus, each pixel is assigned to the class that has the highest probability. Pixels having a probability below a fixed threshold value (95%) were not classified (Chuvieco 1996).

The selected variables had a normal distribution according to a multivariate model (with an equal dispersion matrix for each region), and the Mahalanobis D^2 between each pair of regions was calculated. Then a classification function for each region was obtained. Each function can be expressed by: $Y = ax_1 + bx_2 + \dots + nx_n - k$; where x_1, x_2, \dots, x_n are the values for the variables, a, b, \dots, n are their respective coefficients, and k is the constant for each function. The classification accuracy was evaluated by comparing the predicted class membership of the training sites with their original epidemiological assignments.

Results

The environmental signatures that describe the characteristics of each training class for the epidemic, historic, and nonendemic regions are shown in Table 1. Variability within each epidemiological grouping was expressed by maximum and minimum standard deviation values. The averages of PC2 and PC3 of NDVI, PC3 of LST, and PC3 of precipitation differed among the regions. The variable PC2 of NDVI (or the temporal variation of vegetation in cycles of winter–summer) showed a greater variation (standard deviation) in the nonendemic region than in the other two regions. The nonendemic area had a higher proportion area of summer crops, where the variation in NDVI annual ranges was high. In historic and epidemic areas, where there were summer and winter crops or large areas of perennial crops and grasslands, the annual variation in NDVI was lower. On the other hand, the average of PC3 of precipitation (or temporal variation in precipitation in cycles of spring–autumn) was more different in the historic region than in the other two regions. PC3 of LST showed differences among epidemic region and the other two regions. The PC1 of precipitation, NDVI and LST and the DEM were similar among the three regions.

Using transformed divergence separability measures (or Jeffries–Matusita distances), the comparison among sites with different AHF epidemiological situations showed a good separability among the various pair-wise combinations. The highest distance value corresponded to the epidemic versus nonendemic comparison (1.9999), followed by historic versus nonendemic (1.9981), and

Table 1 Environmental signatures that describe the environmental characteristics of the group of pixels representing each training class for epidemic, historic and nonendemic regions

Variable	Regions												
	Epidemic				Historic				Nonendemic				
	Minimum	Maximum	Average	Standard deviation	Minimum	Maximum	Average	Standard deviation	Minimum	Maximum	Average	Standard deviation	
Precipitation	PC1	0.492	0.528	0.503	0.008	0.493	0.528	0.514	0.008	0.495	0.514	0.504	0.005
	PC2	-0.653	-0.284	-0.426	0.128	-0.633	-0.247	-0.447	0.108	-0.687	-0.187	-0.459	0.125
	PC3	-0.439	0.828	0.566	0.316	-0.439	0.568	0.138	0.300	0.194	0.722	0.422	0.131
NDVI	PC1	1.006	1.148	1.084	0.042	1.095	1.173	1.127	0.022	0.949	1.207	1.089	0.054
	PC2	-2.934	-0.597	-2.016	0.623	-2.734	-0.506	-1.312	0.567	-3.023	-0.125	-1.034	0.740
	PC3	0.031	1.456	0.850	0.396	0.538	2.330	1.356	0.506	1.0085	938	0.840	0.615
LST	PC1	1.028	1.056	1.041	0.008	1.017	1.039	1.033	0.005	1.027	1.053	1.042	0.009
	PC2	-2.145	-1.362	-1.735	0.247	-2.210	-1.444	-1.850	0.208	-2.387	-1.484	-1.929	0.242
	PC3	-0.962	0.970	-0.057	0.535	-1.299	0.323	-0.431	0.462	-0.949	0.171	-0.483	0.344
DEM	0.598	0.665	0.634	0.019	0.598	0.670	0.624	0.016	0.604	0.761	0.629	0.038	

NDVI/ Normalized difference vegetation index, LST land surface temperature, DEM digital elevation model

epidemic versus historic 1.9942. These results show a great differentiation among the considered environmental variables.

The supervised maximum likelihood classification generated the distribution observed in the left panel of Fig. 3. Sites with identical shading had similar environmental characteristics. The epidemic class was circumscribed to a region covering the southern Santa Fe province, southeastern Cordoba province and northwestern Buenos Aires province. The historic class was divided into two geographic groups, a larger one situated in the northeastern Buenos Aires province and a smaller one in the center and southeast of this province. The nonendemic class also showed two groups. One is in the center of the Santa Fe province extending north of the epidemic class, and the second group is in the middle of the historic class groups. The three classes showed a border of contact where pixels of each class were mixed. None of the three classes included pixels belonging to the La Pampa province.

The calculation of D^2 showed significant differences among pairs of regions or areas with different AHF characterizations (epidemic vs. nonendemic: $F = 3.145$, 1 and 35 df , $P = 0.003$; epidemic vs. historic: $F = 6.206$, 1 and 42 df , $P = 0.000003$; historic vs. nonendemic: $F = 7.24$, 1 and 41 df , $P = 0.000000$). Classification functions provided a tool for placing new sites in the existing three classes. The coefficient and the constants for these functions, according to the class, are shown in Table 2. When the classification functions were applied, 83.1% of the sites were correctly reclassified in the original epidemiological class or group (Table 3).

Discussion

Our results identify temporal differences in environmental variables of the regions and a high spatial overlap between the areas defined by the epidemiological AHF situation and our areas classified from environmental variables. These data translate the positive association between *C. musculus* population density and AHF epidemiological situations into a spatial dimension.

The study area is physiognomically recognized as an agroecosystem where agricultural expansion was great during the period 1950–1980. This agricultural expansion involved changes in types of farming and agricultural management practices. The changes have generated different zones in the cultivated area. In the central pampean region, annual crops (summer cycled annual and winter cycled annual) replaced perennial, and in the crop field areas of the Espinal, annual crops replaced the natural (or native) vegetation (Paruelo et al. 2005).

Annual crops have a well-defined growing season, shorter than grasslands, followed by a fallow period, with a very low or null leaf area index. According to Paruelo et al. (2001), the information derived from

Fig. 3 *Left* Graphic register of the AHF endemic area (epidemic and historic areas) and nonendemic area, generated by the method of supervised classification. *Right* The endemic area graphic presented by Sabbatini and Maiztegui (1970)

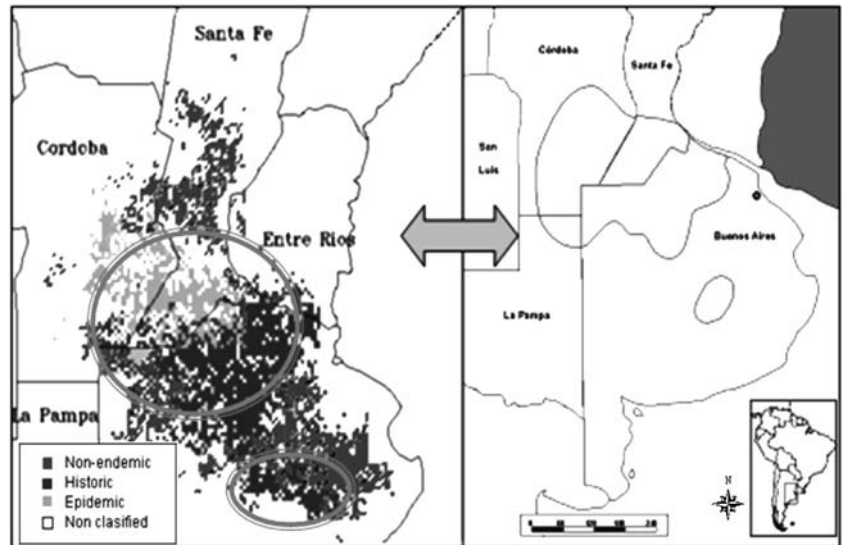


Table 2 Classification functions for each epidemiological area

Variables	Nonendemic Coefficients	Endemic Coefficients	Historic Coefficients
PC1_precipitation	100,106.2	99,776.9	99,786.5
PC2_precipitation	39.8	41.0	33.6
PC3_precipitation	2,331.8	2,323.8	2,316.9
PC1_NDVI	-4,210.7	-4,189.9	-4,146.2
PC2_NDVI	429.5	425.3	424.9
PC3_NDVI	-181.3	-179.7	-178.2
PC1_LST	6,344.7	6,311.9	6,243.0
PC2_LST	7.2	9.3	6.5
PC3_LST	-2.1	-2.1	-2.0
DEM	6,228.7	6,204.4	6,254.0
Constant	-28,379.5	-28,186.3	-28,207.6

PC Principal component, NDVI normalized difference vegetation index, LST land surface temperature, DEM digital elevation model

remotely sensed data can accurately represent functional attributes of the ecosystem, such as aboveground net primary production, and suggests that the NDVI traits used have a clear biological meaning. Paruelo et al. (2001) determined that in the southern pampa, NDVI peaked early (October–November), whereas in the northeastern pampas, NDVI peaked in late summer (February). These authors (Paruelo et al. 2001) observed areas with sharp differences in the timing of the NDVI peak associated with different agricultural systems, and Guerschman et al. (2003) showed important differences in the NDVI dynamics of temperate areas depending on the crop type that replaced the natural vegetation. Thus, the phenological characteristics of the crops in the temperate region of Argentina may explain the range of annual variation in NDVI. In our results, the comparison of the variation in variables among the regions showed that the temporal variation in vegetation between winter–summer (represented by PC2) and

Table 3 Reclassification of sites after application of classification function in comparison to their original epidemiological group

Area	Nonendemic	Epidemic	Historic	Correct percentage
Nonendemic	14	3	2	73.68
Epidemic	2	16	2	80.00
Historic	1	1	24	92.31
Total	17	20	28	83.07

between spring–autumn (represented by PC3) was greater in the nonendemic region than in the other ones. On the other hand, there was greater variation in precipitation and temperature between spring and autumn within the endemic region than in the nonendemic region.

Understanding how environmental variables influence the ecology of hosts in the study area might also help to explain the AHF epidemiology. Slight ecological differences between the endemic and nonendemic areas might explain the differences in the abundance of populations observed by Polop et al. (2007). Many rodent species respond to vegetation composition and structure and show complex patterns of abundance associated with multiple factors (Imhoff et al. 1997). Some authors (Kravetz et al. 1986; de Villafañe et al. 1992) have suggested an association among weather conditions (temperature and rainfall), their temporal variations, the abundance of *C. musculus*, and AHF epidemiology. An increase in the population density of *C. musculus* due to improved habitat availability as well as to a decline in predation and competition as a consequence of farming has been proposed to explain the onset and spread of AHF (Vanella et al. 1964; Kravetz 1978; Kravetz et al. 1986). Kravetz et al. (1986) suggest that AHF is an ecological disease. The environmental differences among sites with distinct epidemiological AHF

characteristics and the reservoir density differences between endemic and nonendemic situations (Polop et al. 2007) reinforce that concept.

Simultaneous monitoring of environmental variables, such as temperature, precipitation and vegetative cover, would provide data on environmental changes that are related to reservoir population changes and subsequently to changes in the risk of human illness (Mills 1999). We can assume that vegetative cover differences among sites with dissimilar epidemiological AHF conditions represent differences in ecological functioning. Thus, *C. musculus* abundance would respond to temporal environmental differences in NDVI, precipitation and LST variables, observed between the endemic and nonendemic regions, and monitoring can help explain differences in risk by identifying environmental differences.

In the epidemic area, environmental conditions (intensive crops, perennial or annual crops with cycles of summer and winter) would allow the establishment of very large contiguous demes with high levels of genetic flow. Polop et al. (2007) postulated that landscapes that exhibit increased continuity of the host population with high densities will also exhibit increased incidence of AHF. The area would act as a continent for the rodent populations, while the high coalescence among them would allow a great flow of the virus and its maintenance in the area (Chiappero 2001). In well-connected populations of an opportunistic reservoir species, we would expect that the rate of transmission might be greater than in other landscapes.

In the nonendemic area, the environmental conditions (mainly native vegetation or summer-cycle annual

crops) would determine that the reservoir populations use them in a specific space and time, acting as spatial or temporal islands in the area. In these areas, the virus can infect a local host population, but if the population does not maintain its abundance over a certain level, the virus infection cycle can be stopped for the following year's population. Thus, we could subdivide the area into three zones: (1) zone where the population is small and more separated, with little or no genetic flow, (2) a transition zone, where populations are large, less separated and there is little genetic flow, and (3) continents, where populations are larger and can coalesce.

The analyses indicated that a combination of detailed and continuing field information with remotely sensed information and spatial analyses can increase our understanding of AHF epidemiology.

It could be important to identify what habitat factors affect the abundance of different species and the incidence of AHF. Studies relating environmental factors to infection by AHF will be the subject of detailed future studies.

If we want to make a valid assessment of the effects of environmental changes on AHF epidemiology, and considering the lack of human cases as epidemiologic indicators, we need to study further the infection in reservoirs and to prove the epidemiologic-environmental hypothesis proposed.

Acknowledgments We thank M. R. Feuillade for the list of sites with different epidemiological characterizations of AHF. We also acknowledge the critical revision of the manuscript and the assistance with the English version by Dr. Kenneth McGwire.

Appendix

Table 4 The location of each site and its assignment to an epidemiological region

Sites	Regions	Latitude (–)	Longitude (–)	Sites	Regions	Latitude (–)	Longitude (–)		
1	Guatimosin	E	33.28	62.26	34	G. Pinto	H	34.46	61.52
2	A. Cabral	E	32.29	63.23	35	G. Arenales	H	34.17	61.2
3	Ucacha	E	33.02	63.31	36	A. Dulce	H	34.06	60.24
4	Villa Nueva	E	32.26	63.14	37	Baradero	H	33.49	59.3
5	DelCampillo	E	34.22	64.35	38	Bragado	H	35.07	60.3
6	Uranga	E	33.28	60.68	39	Chillar	H	37.18	59.59
7	Alcorta	E	33.51	61.66	40	Chivilcoy	H	34.54	60.02
8	M. Paz	E	33.53	60.9	41	Chacabuco	H	34.39	60.28
9	J.B. Molina	E	33.48	60.5	42	C. Sarmiento	H	34.11	59.46
10	S. Pedro	E	33.48	59.68	43	Arrecife	H	34.04	60.07
11	S. Nicolás	E	33.35	60.15	44	Los Toldos	H	35	61.02
12	Colón	E	33.54	61.06	45	Azul	H	36.47	59.51
13	S. Teresa	E	34.01	61.54	46	Lincoln	H	34.52	61.33
14	Carmen	E	33.44	61.47	47	Gigena	N-E	32.76	64.35
15	Venado Tuerto	E	33.45	61.59	48	C. Casare	N-E	35.37	61.22
16	Maggiolo	E	33.44	62.14	49	Chucul	N-E	33.02	64.16
17	S. Eduardo	E	33.52	62.06	50	Maciel	N-E	32.46	60.88
18	Arteaga	E	33.05	61.48	51	Oliveros	N-E	32.6	60.86
19	Huanchilla	E	33.4	63.38	52	S. Jorge	N-E	31.54	61.51
20	La Carlota	E	33.25	63.18	53	Piamonte	N-E	32.08	61.59
21	9 de Julio	H	35.27	60.52	54	Los Cardos	N-E	32.2	61.38
22	Ferré	H	34.09	61.09	55	M. Susana	N-E	32.16	61.55

Table 4 (Contd.)

Sites	Regions	Latitude (–)	Longitude (–)	Sites	Regions	Latitude (–)	Longitude (–)		
23	Olavarría	H	36.53	60.2	56	El Trebol	N-E	32.12	61.43
24	Vedia	H	34.3	61.33	57	Galvez	N-E	32.03	61.13
25	Tandil	H	37.19	59.08	58	Coronda	N-E	31.58	60.55
26	Salto	H	34.18	60.15	59	C. Pellegrini	N-E	32.03	61.48
27	S. Regina	H	34.34	63.1	60	C. Rosquin	N-E	32.03	61.36
28	Zárate	H	34.03	59.01	61	Saladillo	N-E	35.38	59.47
29	Melo	H	34.35	63.43	62	T. Lauquen	N-E	35.58	62.44
30	Rojas	H	32.2	60.73	63	R. Perez	N-E	35.24	59.2
31	Pergamino	H	33.57	60.34	64	G. Alvear	N-E	36.01	60.01
32	Roberts	H	35.09	61.58	65	C. Tejedo	N-E	35.23	62.25
33	G. Villegas	H	35.02	63.02					

N-E Nonendemic, *E* epidemic, *H* historic

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