# CLIMATIC AND DEMOGRAPHIC DETERMINANTS OF AMERICAN VISCERAL LEISHMANIASIS IN NORTHEASTERN BRAZIL USING REMOTE SENSING TECHNOLOGY FOR ENVIRONMENTAL CATEGORIZATION OF RAIN AND REGION INFLUENCES ON LEISHMANIASIS

# R. ALEX THOMPSON, JOSÉ WELLINGTON DE OLIVEIRA LIMA, JAMES H. MAGUIRE, DEWITT H. BRAUD, AND DANIEL T. SCHOLL

Department of Pathobiological Sciences, School of Veterinary Medicine, and Department of Geography and Anthropology, Louisiana State University, Baton Rouge, Louisiana; Fundação National de Saúde/Ceará, Fortaleza, Ceará, Brazil; Department of Immunology and Infectious Disease, Harvard School of Public Health, Boston, Massachusetts

*Abstract.* Remote sensing (RS) permits evaluation of spatial and temporal variables that can be used for vectorborne disease models. A Landsat Thematic Mapper scene covering Canindé, Ceará in northeastern Brazil (September 25, 1986) was spectrally enhanced and classified using ERDAS (Atlanta, GA) Imagine for 873 4-km<sup>2</sup> areas. The population and number of cases of American visceral leishmaniasis (AVL) were determined for each 4-km<sup>2</sup> area. Relative risk (RR) ratios were calculated for climate, demographic, and case data recorded for 17 years by the Municipality of Conidé The RR of AVL for a child less than 10 years old from the foothills relative to non-foothill residency was 4.0 (95% confidence limit = 3.5, 4.5). The RR of AVL in children was 9.1 during a time when the three-year rolling rain average (current year plus two previous year's precipitation) was between 40 and 60 cm relative to rain greater than 100 cm. The results suggest that features detected by RS techniques combined with climatic variables can be used to determine the risk of AVL in northeastern Brazil.

## INTRODUCTION

Historically, 90% of the cases of American visceral leishmaniasis (AVL) in Brazil occurs in the northeastern part of this country, where the highest incidence occurs among children living in foothills of rural areas.<sup>1,2</sup> The protozoa responsible for this disease, *Leishmania chagasi*, which can be isolated from humans, dogs, and foxes, is transmitted by the bite of the female phlebotomine sand fly *Lutzomyia longipalpis* (Diptera: Psychodidae).<sup>3–5</sup> Symptoms of AVL (kala azar) develop after a 2–4-month incubation period, but 6–18 times more people experience asymptomatic infections than symptomatic infections.<sup>6</sup> The treatment of choice is a 28-day course of pentavalent antimony (Sb<sup>5</sup>). Without treatment case fatality approaches 95%.<sup>7</sup>

The sand fly vector is nocturnal, anthropophilic, reproduces best between 23°C and 28°C and a relative humidity of 70–100%, and has a short flight range.<sup>8</sup> It completes its life cycle in 5–8 weeks under ideal conditions.<sup>9</sup> Such specific environmental conditions required for vector propagation make leishmaniasis an ideal candidate for study using remote sensing (RS) by satellite.<sup>10,11</sup>

Remote sensing, image processing, and geographic information systems (GIS) are computer programs designed to collect, store, and analyze data relative to geographic locations. They are being used more frequently in public health studies to identify, classify, and organize environmental variables that influence vector distribution and abundance.<sup>12</sup> Satellite-borne sensors measure reflected electromagnetic and emitted thermal energy, and algorithms are available to classify data into surrogate indices for surface vegetation, moisture, or dryness.<sup>11,13</sup> These indices are used in GIS and in statistical models to define associations between climate and the incidence of vector-borne disease. Investigations have used RS/GIS technology to study leishmaniasis and climate in the Middle East, the ecology of malaria in sub-Saharan Africa, environmental determinants of Rift Valley Fever virus infection in Kenya, and risk for Lyme disease in the United States.11,13-19

In this study, RS and GIS were used to separate the environment into foothills or plains categories with electromagnetic spectral analysis of vegetation to evaluate the effect of age and precipitation by region on the incidence of AVL in the municipality of Canindé (Ceará State), Brazil.

# MATERIALS AND METHODS

**Study area.** The municipality of Canindé, with an area of 2,883 km<sup>2</sup>, is located 113 km inland from Fortaleza, the coastal capital of Ceará, Brazil. Canindé, the administrative center of the municipality, is situated at  $4^{\circ}27'32''S$ ,  $39^{\circ}18'32''W$ . It has an altitude of 150 meters above sea level and is situated on a plain between small mountains in the municipality of Baturité and the foothills of Canindé. The highest peak in Canindé is 1,085 meters above sea level, and most of the plateaus in the foothills range between 300 and 600 meters above sea level.

The climate is biseasonal with a seven-month dry season and a five-month rainy season during normal years. The mean daily maximum and minimum temperatures are  $30^{\circ}$ C and  $24^{\circ}$ C, respectively, with larger diurnal variations than the variations in mean monthly temperatures. The annual average rainfall is 756 mm, ranging from a minimum of 191 mm in 1993 to the maximum of 1,678 mm in 1985.<sup>20,21</sup> The population of the municipality increased from 50,652 people in 1970 to 61,650 people in 1991, during which time there was extensive migration from the rural zone to the cities Canindé and Fortaleza.<sup>20</sup> There has been little immigration into the municipality from other regions, and it is estimated that 98% of the residents of Ceará live in their municipality of birth.<sup>20</sup>

**Study design.** A retrospective cohort study encompassing 17 years was designed in which the units of observation were  $2 \text{ km} \times 2 \text{ km} (4 \text{ km}^2)$ -inhabited areas of land within the municipality. This unit of observation was chosen because of the short flight range of sand flies, the spatial resolution (30 m<sup>2</sup>) of Landsat Thematic Mapper (TM) satellite scenes, the 2 km  $\times$  2 km resolution of the 1:100,000 universal transverse mer-

cator map used to produce a digitized map of Canindé, and the imprecise spatial location of houses in this region. Each case of AVL in children less than 10 years old (childhood AVL) diagnosed between January 1981 and December 1997 by health care physicians of the Fundação Nacional de Saúde of Ceará (FNS/CE) was allotted to a 4-km<sup>2</sup> area by the address given in the clinical history. Associations between the estimated incidence density of childhood AVL and environmental, temporal, geographic, and climatic factors were estimated using multivariate logistic regression.

**Subjects.** Annual disease summary reports from 1981 to 1997 containing data on 333 cases of AVL were provided by the FNS/CE in Fortaleza. Each case record included the name or initials of the patient, gender, age, address, date of diagnosis of AVL, and procedures and criteria used to establish the diagnosis. The use of case data in this project was approved by the FNS/CE.

The ERDAS (Atlanta, GA) Imagine Area of Interest tool and a map of Canindé were used to create an image grid of the 873 squares ( $2 \text{ km} \times 2 \text{ km} [4 \text{ km}^2]$ ) that covered the entire area of the municipality.<sup>22,23</sup> The location of each of the 475 localities (subdivisions) of the municipality was determined on the grid, the 1991 list of houses from the FNS/CE Chagas control program was used to assign each house to a  $2 \text{ km} \times 2$ km square. A total of 292 squares contained the 475 localities, including five squares that included the city of Canindé. The child population of each square over the 17-year period was determined from the number of infants entering the cohort at birth and exiting at age 10 years. During this period, there were 333 cases of AVL of which 71 (21.3%) were excluded from the project because of an age greater than 10 years (56 people) and an incorrect address (15 people).

**Population-at-risk.** Population-at-risk (PAR) values for the city, plains, and foothills were estimated from the 1980 and 1991 census data. The annual PAR estimate for each 4-km<sup>2</sup> square was derived by counting the number of houses per square in 1980 and 1991, multiplying the number of houses per square by 3.65 (mean number of people per house in 1981) or 3 (mean number of people per house in 1991), and calculating the value for the intervening years by interpolating using methods described in this report. The PAR estimates were multiplied by the percentage of the population less than 10 years in the city (30.9%) and the rural areas (29.95%) to derive the childhood PAR estimates.<sup>20</sup> Each childhood case of AVL was assumed to contribute a half year of risk during the year of diagnosis, but no subsequent risk.

**Climate.** Precipitation data collected in the city of Canindé (sole official source) from 1973 through 1997 were supplied by the Fundação Cearense do Meteorologia e Recursos Hidricos (FUNCEME).<sup>21</sup>

**Satellite data.** Using ERDAS Imagine, the grid of 873 individual 4-km<sup>2</sup> squares was overlaid on a 400-mb Landsat TM scene of the region (resolution = 30 meters, seven bands, obtained on September 25, 1986; Earth Resources Observation Systems Data Center, Sioux Falls, SD) during the dry season of 1986.<sup>22,23</sup> The Landsat scene was georeferenced using coordinates taken from 33 locations by a Magellan global positioning system (GPS) unit between September 10 and 25, 1997, and rectified with a second-order polynomial transformation, in which the root mean square error was less than one.<sup>22</sup> By visual inspection, all the Magellan GPS coordinates on the transformed image fell within 500 meters of the location at which the GPS coordinated were recorded.

The selected satellite image from the dry season (September 25, 1986) had cloud cover, cloud shadows, and shadows that would strongly alter the values of RS indices for each 4-km<sup>2</sup> square if these influences were not removed by the procedure described in this report.<sup>22</sup> The combination of Landsat electromagnetic spectral bands 4, 5, and 3 (near infrared, mid-infrared, and visible green), which emphasize growing vegetation, were used to determine the areas in the municipality that were covered with clouds, cloud shadows, shadows, and actively growing vegetation.<sup>22,24</sup> Using this three Landsat band combination, pixels were classified into 100 spectral classes by applying the ERDAS Imagine ISODATA iterative cluster analysis and classification algorithm.<sup>22</sup> The 100 class isodata image was overlaid on the original rectified image; areas with clouds, cloud shadows, and shadows were removed from the image following standard to facilitate image analysis.<sup>22</sup> The cloud, cloud shadow, and shadow areas were removed from the satellite images before processing by the ERDAS normalized difference vegetation index (NDVI) and tasseled cap (TC) algorithms to determine of each 4-km<sup>2</sup> square's mean RS index values for actively growing vegetation.

Each 4-km<sup>2</sup> square was classified as city, plains, foothill, or neither from the resulting masked satellite image by reclassifying areas of 200 pixels (approximately 20 hectares) into one of four classes (foothills, plains, city, and other [roads, mining slag heaps, and water reservoirs]) by a supervised classification scheme using the Landsat TM 4-5-3 band combination supplemented with visual comparison of the 4-5-3 band image and use of location, altitude information, maps, and site visits. IMAGINE software was used to overlay the grid of 4-km<sup>2</sup> squares on the 1986 Landsat scene to determine the proportion of the four classes in each square and then categorizing each 4-km<sup>2</sup> square as foothill, city, or plains if more than 50% of the area fell into one of the classes or manually based on the largest percentage class category in each square by visual inspection.

Sensitivity analysis of PAR estimates. Because census data were available only for 1980 and 1991 and the yearly rate of change in population was not known for the 17 years between 1981 and 1997, six scenarios were considered to calculate the annual PAR estimates. Model 1 (straight line interpolation or SLI) determined the annual population estimate by dividing the percent change from the 1980 population to the 1991 population by 11 and adding that amount to the previous year's estimate. Model 2 assumed that the populations were constant for each region except in 1984 and 1994, when droughts provoked mass migration from the rural areas into the city of Canindé. Model 3 (migration return model) assumed a 25% reduction in rural population and a 25% increase in the urban population in both 1984 and 1994. After two years, 10% of the population and, during the fourth and fifth years, an additional 5% returned to the rural area, and thereafter the rural and urban populations followed the SLI population numbers. Models 4 and 5 incorporated a 10% and 25% random-number-generated annual variation about the SLI line, respectively. Model 6 assumed a 25% urban and a 10% rural random-number-generated variation about the SLI lines.

Statistical analysis. Statistical analyses used SPlus 4.5

(Mathsoft, Inc., Seattle, WA), S + Spatial Stats (Data Analysis Products Division; Mathsoft, Inc.), and EGRET for Windows 2.0.31 (Cytel Software Corporation, Cambridge, MA). Poisson regression models using the maximum likelihood method were used to estimate the associations between the independent rainfall, time period, and region variables with the cases of AVL in each 4-km<sup>2</sup> square, and deviances were used to compare the goodness-of-fit for the various models. Age and gender distributions were tested with chi-square tests for homogeneity. Serial and time autocorrelations were tested with Yule-Walker equations. ArcView GIS (Environmental Systems Research Institute, Inc., Redlands, CA) graphics were used for manipulation and data querying. Age and gender distributions were tested with chi-square tests for homogeneity. ArcView GIS (Environmental Systems Research Institute, Inc.) was used for manipulation and data querying.

#### RESULTS

The population of the municipality increased by 4% from 1981 to 1991 (Table 1). There was a 1.7% overall increase in the child population of the municipality from 16,970 in 1981 to 17,257 in 1991, during which time the child population of the foothills decreased by 22.7%. Children less than 10 years old contributed only 29% of the total PAR years, but accounted for 82.4% of the cases of AVL during this time. Cases were not autocorrelated serially or by time based on Yule-Walker equations (P = 0.05). During the 17-year period, the estimated crude incidence rate of AVL for Canindé (30.2 cases/ 100,000 person-years [PY]) was seven times greater than that for the entire state of Ceará (4.2 cases/100,000 PY). The number of cases of AVL in Canindé municipality ranged from three cases in 1997 to 61 cases in 1982 (Figure 1), with a peak crude incidence of 102 cases/100,000 PY in 1982, when 60 cases were reported.

The incidence density of childhood AVL was roughly four times greater in the foothills (238/100,000 PY) than in the city (46/100.000 PY) and plains (55/100.000 PY) (Table 1). In general, rates were not significantly greater for boys or girls, although more boys than girls had AVL in the foothills (P =0.05). Overall, children were 11.4 (95% confidence limit = 9.9, 13.2) times more likely to have AVL than adults in Canindé.

The six population models (Figure 2) were used to test the robustness of the data by varying the PAR estimates. The largest variation among the six models was seen for the foothills in 1992, with estimates ranging from a low of 2,556 persons to a high of 4,573; the differences between models also approached 50% in 1984 and 1992. The magnitude of variation in the city and plains population-simulation estimates was similar to that in the foothills. Person-years derived from model 1 were used to calculate age-specific incidence densities (ID) (Figure 1). The ID for each of these six models was used to calculate yearly relative risk (RR) for the risk of childhood kala azar in the foothills and plains relative to the city (Table 2). The variation each year among the six RRs (RR for the risk of kala azar in the foothills compared with that in the city) is shown in Figure 3. This RR approached unity only in years with low numbers of cases (1987, 1988, 1993, and 1996).

Precipitation data were collected from 1973 through 1997 in the town of Canindé but not in the outlying rural areas. The average rainfall from 1981 to 1997 was 671 mm/year (range = 191 mm in 1993 to 1,678 mm in 1985). The incidence and precipitation data lacked time or serial autocorrelation in time lags from one to five periods at the P = 0.05 significance level based on Yule-Walker equations. The three-year rolling rainfall average (current year plus two previous year's precipitation) and the yearly childhood incidence density of AVL in the foothills are shown in Figure 4. Rates of AVL were higher for all periods with rainfall < 90 cm/year compared with those > 90 cm/per year (Table 2), and were highest for periods with < 40 cm/year. The estimated RR for time periods with rainfall between 40 cm and 60 cm versus time periods with rainfall > 90 mm ranged from 8.7 to 9.3 (Table 2). For all six models, the deviance and goodness-of-fit statistics were above the P = 0.05 level and demonstrated that all models adequately fit the data. All explanatory variables had significant Wald statistics (P < 0.05), for except the time period variable. The inclusion of the time period variable in the models was required for acceptable score and -2 log L statistics (P < 0.05).

### DISCUSSION

Our data indicate that AVL in the municipality of Canindé principally affects children living in the foothills of rural areas. Its occurrence is cyclical and inversely related to the rolling three-year-precipitation average. In this study, the crude incidence rate of AVL among children was 11 times greater than that among older persons, and the risk of AVL

Table 1	
---------	--

Childhood and adult population of Canindé municipality and risk of American visceral leishmaniasis (AVL) (1981–1991 Canindé municipality regional demographics and Fundação Nacional de Saúde of Ceará visceral leishmaniasis annual summary)

Region	Number of squares per region*	Population 1981†	Population 1991†	Adult person-years‡	Children person-years‡	Total cases of AVL No. (%)§	Cases of childhood AVL No. (%)§	Total AVL ID¶ cases/100,000	Adult AVL ID¶ cases/100,000	Children AVL ID¶ cases/100,000	Relative risk children/adult and 95% confidence intervals
City	5	20,289	30,023	356,113	126,727	79 (25)	58 (22)	16.4	5.9	45.8	7.8 (6, 10)
Plains	168	22,862	18,513	229,704	106,880	67 (21)	59 (23)	19.9	3.5	55.2	15.9 (11, 23)
Foothills	121	15,871	12,856	161,384	72,285	172 (54)	145 (55)	73.6	16.7	200.6	12.0 (9.7, 14.8)
Total	295	59,392	61,392	747,201	305,892	318	262 (82)	30.2	8.3	85.7	11.4 (9.9, 13.2)

\* Number of 2 × 2 km<sup>2</sup> areas located in each region defined with ERDAS from 1974 Universal Transverse Mercator Map. † IPLANCE (Fundação Instituto de Planejamento do Ceará) 1980 and 1991 census data (population estimates based on straight-line extrapolation from 1980–1991 IPLANCE data). Person-years determined by population in age group per région multiplied by number years at risk.
§ Fundação Nacional de Saúde of Ceará Annual Summary, all cases with a municipality address.
¶ Incidence density (ID) per 100,000 person years based on number of cases divided by person-years multiplied by 100,000.

# Relative risk of visceral leishmaniasis in Canindé for children relative to adults.



FIGURE 1. Incidence densities of adult and childhood American visceral leishmaniasis (AVL) in Canindé, Brazil, 1981–1997.

in children from the foothills was four times that of children living in the plains or city.

In Canindé, 82% of the AVL cases occurred among children less than 10 years old, a figure consistent with the 70% and 80% incidence of AVL in children nine years old or less reported by Badaró and others<sup>25</sup> and Harrison and others,<sup>26</sup> respectively. As far back as 1956, Deane<sup>3</sup> concluded that AVL was primarily a disease of children in the state of Ceará, and 36 years latter, Evans and others<sup>27</sup> arrived at the same conclusion. Jeronimo and others reported that even in urban areas such as Natal, Brazil children comprise the majority of AVL cases.<sup>1</sup>

The literature also supports our finding that most (54%) AVL cases occur in the foothills. Evans and others<sup>27</sup> reported that 53% of the AVL cases occur in the foothills and mountains, while Deane<sup>3</sup> and Jeronimo and others<sup>1</sup> reported that AVL most often occurs in the foothills. Little is known about the environmental requirements of the sand fly vector, but Lu. longipalpis has been found most often in brush land or around cultivated fields, and not in open savanna grasslands or heavily forested areas. Sand fly abundance is high in peridomestic areas near maize or bean fields, in areas with large numbers of dogs, or in focal areas of high humidity. These features are typical of caatinga-covered foothills in Canindé.<sup>28-33</sup> The foothills have more foci of high humidity than the plains because of elevation, cloud cover, and slope effect. Cooler temperatures are associated with increased relative humidity and shadows from the hills (north slope effect) and persistent cloud cover results in these cooler areas.<sup>33,34</sup> Cloud cover over Canindé is so heavy that only two Landsat TM satellite scenes (September 25, 1986 and July 26, 1993) from

approximately 350 scenes (with time between scenes of at least 16–18 days) captured over a 17-year period were sufficiently cloud free to be useful, and both images were taken during the dry seasons of 1986 and 1993.

The 10-year disease cycle that we report is similar to that reported by Deane in Ceará,<sup>3</sup> but twice the 4–5-year AVL cycle length reported by Badaró and others in Jacobina, Bahia, Brazil.<sup>25</sup> It is difficult to explain the cyclic incidence of AVL because much of the important parasite-vector-hostenvironment relationship is unknown and the abundance of Lu. longipalpis varies greatly over space and time for unexplained reasons. Several major differences between Canindé and Jacobina may explain the different cycles of AVL. Jacobina is an urban area with a population exceeding 40,000 people and substantial immigration, while Canindé is rural, with 98% of its 55,000 residents in 1986 born in the municipality. Jacobina has biannual rainy periods, while Canindé at most has rain during a three- or four-month period each year; some years, there is little or no rainfall. Occasionally, the interior areas of Ceará have droughts that may last for 3-5 years and drastically affect disease patterns.

The inverse relationship between the incidence of AVL and the three-year-precipitation average has not been previously reported. Travi and others<sup>32</sup> and Morrison and others<sup>29,30</sup> reported that the numbers of *Lu. longipalpis* decrease during the rainy season and are most commonly seen in semiarid areas. Even during the rainy season, Canindé is semiarid because the small amount of rain that does fall is concentrated in a localized area for only a few days, which makes the conditions ideal for the sand fly.<sup>33,34</sup>

It is not surprising that a 40-60-cm, three-year-precipi-



FIGURE 2. Canindé foothills (1981–1997). Model 1: • Straight line interpolation (SLI) Model 2: 🗆 Mass migration without return Model 3: ■ Mass migration with return to the SLI Model 4: ◆ 10% variation about the SLI Model 5: ▲ 25% variation about the SLI Model 6: □ 25% urban 10% rural random number variation about the SLI Model.

tation average in an equatorial-semi-arid area of poor soils would predispose children to malnutrition because of decreased food production, exhaustion of household savings, and overall hardship. The low three-year-precipitation average describes a drought period and in poor, rural, agricultural areas of Brazil, droughts (secas) stimulate migration to urban areas and concentrate people around water supplies.<sup>33</sup> A positive association between malnutrition, which increases susceptibility to disease, and increased incidence of AVL in children has been documented in the literature by Evans and others in rural Ceará,27 Badaró and others in Jacobina,25 and Harrison and others in Sobral, Ceará.<sup>26</sup> During droughts, families concentrate around the remaining watered areas in the foothills, as do other potential reservoir hosts and sand flies, which take advantage of the foci of high humidity to complete their development. The negative relationship between AVL incidence and three-year-precipitation could be explained by drawing together malnourished children, parasites and vectors in the foothills.

Determination of age-specific rates for AVL in this study was impossible because census data were only available in approximately five-year increments. Nevertheless, our estimates of rates ratios were remarkably similar in six different population models tested, all of which were robust over a 50% variation in the underlying population (Thompson RA, unpublished data). Our target population was limited to children to reduce a dilution effect that would result from combining the low incidence rate of older people with the high rates of children. Focusing on children also may have reduced misclassification errors arising from migration, since children are less likely to migrate than adults.<sup>12</sup>

Because of the retrospective nature of the study, clinical diagnostic techniques could not be evaluated, but during the study period diagnostic procedures and reporting tools used

TABLE 2

American visceral leishmaniasis (AVL) relative risk (RR) ratio comparisons for explanatory variables in Poisson regression models based on six population simulation models Canindé municipality, 1981-1997\*

	Logistic regression Canindé municipality parameter odds ratios									
Parameter	Model 1 RR (CL)	Model 2 RR	Model 3 RR	Model 4 RR	Model 5 RR	Model 6 RR				
Foothills†	4.0 (3.5, 4.5)	4.19	4.48	3.71	4.09	3.9				
Plains†	0.8(0.5, 1.3)	1.32	1.46	1.02	1.22	1.19				
Time period <sup>‡</sup>	0.76(0.6, 1)	0.77	0.78	0.69	0.75	0.81				
Rain 2§	3.07 (1.4, 8.1)	3.01	2.89	3.05	3.15	3.11				
Rain 3§	9.1 (4.4, 23)	8.74	8.66	9.33	9.10	9.17				
Rain 4§	9.2 (4, 25)	8.04	8.32	9.59	9.19	9.32				

\* Values are relative risk ratios of childhood AVL incidence rates (95% confidence limits).

† Compared to rates in the city. ‡ Time period (1989–1997) vs. base time period (1981–1988) § Three-year rolling rainfall averages > 60 and < 90 cm (Rain 2), > 40 and < 60 cm (Rain 3) and  $\leq$  40 cm (Rain 4), respectively. Cut-offs of 40, 60, and 90 correspond to natural breaks in average rainfall. Relative risk ratios are from comparisons with rolling rainfall averages > 90 cm (Rain 1)



FIGURE 3. Childhood relative risk ratios of American visceral leishmaniasis (AVL) in the foothills versus the city of Canindé, Brazil, 1981–1997.

by the FNS/CE were standardized. The probability of underreporting cases was low because most residents know about AVL and that the antimonial therapy was free and available only through the FNS/CE. Moreover, most families in Canindé were poor and would elect local free care from the FNS/ CE rather than care in private hospitals in Fortaleza. Furthermore, our reported RR for AVL in foothill residents compared with the plains or city residents has a greater probability of understating the RR because the foothills are more isolated and inaccessible to the FNS/CE personnel than the plains or city regions and the chance for an AVL case to be undiagnosed was highest.

The statistical associations of this study were influenced by the spatial relationships between the incidence of AVL and demographic, climatic, and environmental explanatory variables. The precision and strength of the statistical associations depended on homogenous stratification of the regional variables and accurate determination of the population-at-risk for each region. By enhancing satellite images and classifying the vegetative reflectance with RS, we achieved greater accuracy in the assignment of the 4-km<sup>2</sup> squares and their residents to the correct stratum, thereby reducing misclassification errors and increasing precision and strength of statistical associations.

Few studies have tracked the incidence of visceral leishmaniasis (Old or New World) over time and correlated the incidence rate with environmental or climatic factors. The work of Cross and others<sup>14</sup> in the Middle East demonstrated increased rates of visceral and cutaneous leishmaniasis with increased mean monthly temperature and NDVI values. This study did not differentiate between visceral and cutaneous disease, counted both prevalent and incident cases, used advanced very high resolution radiometer (AVHRR) course spatial resolution data (7.6-km<sup>2</sup> pixel), took place in a region with major seasonal temperature variations, and used intrayear, not inter-year, comparisons. Nevertheless, our finding of a strong association between foothill-type vegetation during periods of normal rainfall agrees with the association with vegetation factors that they reported.

In the Sudan, Thompson and others refined their logistic regression model, which used environmental variables (rainfall, temperature, soil type, and NDVI) to predict the presence of Phlebotomus orientalis (vector of visceral leishmaniasis), by delineating the areas where P. orientalis may occur with a rainfall boundary based on the distribution of Acacia-Balanites woodland.<sup>11</sup> In his work, they demonstrated that the important ecologic parameters in the statistical model were mean annual maximum daily temperature and soil type. He further stated that P. orientalis is associated with Acacia-Balanites woodland. In this study, they used temporally and spatially coarse data to build their statistical model: AVHRR data (5-km spatial resolution), digital maps (resolution =1:1,000,000), and two-day sand fly collection periods during a three-month period in 1996. This area had variations in mean annual temperature but little variation in rainfall (areas on the north boundary receive < 400 mm of annual rainfall). In contrast, Canindé had little variation in mean annual temperature, but larger variations in rainfall (191-1,678 mm). Again, our finding a positive association between foothilltype vegetation and the incidence of AVL agrees with the



FIGURE 4. Childhood incidence density of American visceral leishmaniasis (AVL) and the three-year rolling rainfall average in Canindé, Brazil, 1981–1997.

Sudan data and points to the importance of vegetation in the environment that supports AVL.

The next step in determining environmental and climatic determinants of risk of AVL would be to use finer spatial resolution and a prospective study design; ideally, a nested case-control design. Such an approach would provide actual data on population numbers, age and gender, immunologic status of the population, and local climatic factors that are important in the AVL life cycle.

Acknowledgments: We thank the professionals, office staff, and field personnel of Fundação National de Saúde/Ceará for the assistance with these studies.

Financial support: This work was supported by grant AI-16305-13 from the National Institutes of Health (Harvard University), internal support from School of Veterinary Medicine at Louisiana State University, and Fundação National de Saúde/Ceará, Fortaleza (Ceará, Brazil).

Authors' addresses: R. Alex Thompson, Faculté de Médecine Vétérinaire, CP 5000, Saint-Hyacinthe, QC, J2S 7C6 Quebec, Canada, Telephone: 450-773-8531, Fax: 450-778-8120, E-mail: alex.thompson@ umontreal.ca. José Wellington de Oliveira Lima, Fundação National de Saúde/Ceará, Rua Joaõ Cordeiro 1013/103, 60.110-300 Fortaleza, Ceará, Brazil, E-mail: jlima@fortalnet.com.br. James H. Maguire, Parasitic Diseases Epidemiology Branch, Division of Parasitic Diseases, Centers for Disease Control and Prevention, Mailstop F-22, 4770 Buford Highway NE, Atlanta, GA 30341-3724, Telephone: 770-488-7766, Fax: 770-488-7761, E-mail: jmaguire@cdc.gov. DeWitt H. Braud, Department of Geography and Anthropology, 227 Howe-Russell Geoscience Complex, Louisiana State University, Baton Rouge, LA 70803, Telephone: 225-578-6177, Fax: 225-578-4420, Email: dbraud1@lsu.edu. Daniel T. Scholl, Department of Pathobiological Sciences, School of Veterinary Medicine, Louisiana State University, Baton Rouge, LA 70803, Telephone: 225-578-9653, Fax: 225-578-9655, E-mail: echdts@lsu.edu

#### REFERENCES

- Jeronimo SMB, Oliveia RM, Mackey S, Costa RM, Sweet J, Nascimento ET, Luz KG, Fernandes MZ, Jernigan J, Pearson RD, 1994. An urban outbreak of visceral leishmaniasis in Natal, Brazil. *Trans R Soc Trop Med Hyg 88*: 386–388.
- Pearson RD, Sousa AQ, 1996. Clinical spectrum of leishmaniasis. *Clin Infect Dis 22:* 1–13.
- Deane LM, 1956. Leishmaniose Visceral no Brasil. Rio de Janeiro: Serviço National de Educação Sanitária, 81–121.
- Kettle DS, 1990. Trypanosomiases and Leishmaniases. Kettle DS, ed. *Medical and Veterinary Entomology*. Wallingford, United Kingdom: CAB International, 580–587.
- Ferro C, Morrison AC, Torres M, Pardo R, Wilson ML, Tesh RB, 1995. Age, structure, blood-feeding behavior, and *Leishmania chagasi* infection in *Lutzomyia longipalpis* (Diptera: Psychodidae) at an endemic focus of visceral leishmaniasis in Colombia. J Med Entomol 38: 618–629.
- Silveria TF, Shaw JJ, Bichara CNC, Costa JML, 1997. Leishmaniose visceral Americana. Queiroz de Leão RN, ed. *Doenças Infecciosas e Parasitárias Enfoque Amazôico*, Belém, Brazil: Cejup:UEPA: Instituto Evandro Chagas, 632–644.
- Berman JD, 1996. Human leishmaniasis: clinical, diagnostic, and chemotherapeutic developments in the last 10 years. *Clin Infect Dis 24*: 684–703.
- el Sawaf BM, El Sattar SA, Shehata MG, Lane RP, Morsy TA, 1994. Reduced longevity and fecundity in *Leishmania*-infected sand flies. *Am J Trop Med Hyg 51*: 767–770.
- 9. Tang Y, Ward RD, 1998. Sugar feeding and fluid destination control in phlebotomine sandfly *Lutzomyia longipalpi* (Deptera: Psychodidae). *Med Vet Entomol 12*: 13–19.
- 10. Hay SI, Tucker CJ, Rogers DJ, Packer MJ, 1996. Remotely sensed surrogates of meteorological data for the study of the

distribution and abundance of arthropod vectors of disease. Ann Trop Med Parasitol 90: 1–19.

- 11. Thompson MC, Elnaiem DA, Ashford RW, Connor SJ, 1999. Toward a kala azar risk map for Sudan: mapping the potential distribution of *Phlebotomus orientalis* using digital data of environmental variables. *Trop Med Int Health 4*: 105–113.
- Hay SI, Packer MJ, Rogers DJ, 1997. The impact of remote sensing on the study and control of invertebrate intermediate hosts and vectors of disease. *Int J Remote Sensing* 18: 2899–2930.
- 13. Avery TE, Berlin GL, 1992. Fundamentals of Remote Sensing and Airphoto Interpretation. Fifth edition. Upper Saddle River, NJ: Prentice-Hall, Inc., 201–287.
- Cross ER, Newcomb WW, Tucker CJ, 1996. Use of weather data and remote sensing to predict the geographic and seasonal distribution of *Phlebotomus papatasi* in Southwest Asia. Am J Trop Med Hyg 54: 530–536.
- 15. Lunetta RS, Cosentino BL, Montgomery DR, Beamer EM, Beechie TJ, 1997. GIS-Based evaluation of salmon habitat in the Pacific Northwest. *Photogram Eng Remote Sensing 63:* 1219–1229.
- Thompson MC, Connor SJ, Milligan PJM, Flasse SP, 1996. The ecology of malarias seen from Earth-observation satellites. *Ann Trop Med Parasitol 90*: 243–264.
- 17. Linthicum KJ, Bailey CL, Tucker CJ, Mitchell KD, Logan TM, Davies FG, Kamau CW, Thande C, Wagateh JN, 1990. Application of polar-orbiting, meteorological satellite date to detect flooding of Rift Valley fever virus vector mosquito habitats in Kenya. *Med Vet Entomol 4:* 433–438.
- Nicholson MC, Mather TN, 1996. Methods for evaluating Lyme disease risks using geographic information systems and geospatial analysis. J Med Entomol 33: 711–720.
- 19. Blan L, West E, 1997. GIS modeling of elk calving habitat in a prairie environment with statistics. *Photogramm Eng Remote Sensing* 63: 161–167.
- 20. IPLANCE, 1995. *Anuário Estatístico do Ceará*. Fortaleza, Ceará, Brazil: IPLANCE.
- 21. FUNCEME, 1998. Anuário Metorologia e Recursos Hidricos Estatístico Do Ceará. Fortaleza, Ceará, Brazil: FUNCEME.
- 22. ERDAS, 1997. *ERDAS Field Guide*. Fourth edition. Atlanta: ERDAS Inc.
- 23. IBGE, 1974. 1974 Universal Transverse Mercator Map, Scale 1:

100,000. Rio de Janeiro: Fimdaòão Instituto Braziliero de Geografia Estatístico.

- Lillesand TM, Kiefer RW, 1994. Remote Sensing and Image Interpretation. Third edition. New York: John Wiley & Sons, Inc., 427–523.
- Badaró R, Jones TC, Lorenço R, Cerf BJ, Sampaio D, Carvalho EM, Rocha H, Teixeira R, Johnson WE Jr, 1986. A prospective study of visceral leishmaniasis in an endemic area of Brazil. J Infect Dis 154: 639–649.
- Harrison LH, Naidu TG, Drew JS, de Alencar JE, Pearson RD, 1986. Reciprocal relationships between undernutriton and parasitic disease visceral leishmaniasis. *Rev Infect Dis 8:* 447– 453.
- Evans TG, Teixeira MJ, McAuliffe IT, de Alencar Barros Vasconcelos I, Wilson Vasconcelos A, de Queiroz Sousa A, Wellington de Oliveira Lima J, Pearson RD, 1992. Epidemiology of visceral leishmaniasis in northeast Brazil. J Infect Dis 166: 1124–1132.
- Cameron MM, Pessoa FAC, Vasconcelos AW, Ward RD, 1995. Sugar meal sources for the phlebotomine sandfly *Lutzomyia longipalpis* in Ceará State. *Braz Med Vet Entomol 9:* 263–272.
- Morrison AC, Ferro C, Morales A, Tesh RB, Wilson ML, 1993. Dispersal of the sand fly *Lutzomyia longipalpis* (Diptera: Psychodidae) at an endemic focus of visceral leishmaniasis in Colombia. *J Med Entomol* 30: 427–435.
- Morrison AC, Ferro C, Pardo R, Torres M, Wilson ML, Tesh RB, 1995. Nocturnal activity patterns of *Lutzomyia longipalpis* (Diptera: Psychodidae) at an endemic focus of visceral leishmaniasis in Colombia. *J Med Entomol* 32: 605–617.
- Quinnell RJ, Dye C, 1994. Correlates of the peridomestic abundance of *Lutzomyia longipalpis* (Diptera: Psychodidae) in Amazonian Brazil. *Med Vet Entomol 8:* 219–224.
- Travi BL, Montoya J, Gallego J, Jaramillo C, Llano R, Velez ID, 1996. Bionomics of *Lutzomyia evansi* (Diptera: Psychodidae) vector of visceral leishmaniasis in northern Colombia. J Med Entomol 33: 278–285.
- 33. da Cunha E, 1957. *Rebellion in the Backlands*. Fifth edition. Chicago: University of Chicago Press.
- Rao VB, de Lima MC, Frachito SH, 1993. Seasonal and interannual variations of rainfall over eastern northeast Brazil. J Climate 6: 1754–1773.