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Urban Leptospirosis in Salvador Brazil: A Case-control Study and an Evaluation of the Case-control Method

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Urban Leptospirosis in Salvador Brazil: A Case-control Study and an Evaluation of the Case-control Method

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Preface

Urban leptospirosis is a disease that occurs in areas of high rodent density and inadequate sanitation, and thus affects the poor nearly exclusively. Recently identified by the Institute of Medicine as one of the "emerging infectious diseases", epidemic, urban leptospirosis is a phenomenon of rapid urbanization and demographic change in Latin America. The following two papers address different aspects of the epidemiology of leptospirosis.

The first paper is a case control study, identifying risk factors for disease acquisition during an urban epidemic in Salvador, Brazil. This study had several important and novel findings: exposures occurred in both residential and occupational settings, and in residential settings, there were nearly as many female cases as male. While this does contribute to our knowledge of the dynamics of leptospirosis, the findings of the case control study are limited.

The second paper addresses the strengths and limitations of the case control study and calls for the use of interdisciplinary directions in epidemiology. I critique the case control model as having an overly individualistic perspective and not accounting for the socio-historical context, thus omitting vital information. A meta-evaluation of the social epidemiological literature assessing the limitations of contemporary epidemiology is presented in order to frame the issues. Finally, a framework that integrates epidemiological and anthropological perspectives for studying leptospirosis is proposed.

Acknowledgments

I would like to thank Dr. Lee Riley for serving as my thesis mentor in Berkeley and for affording me the opportunity to work in Salvador. I also would like to thank Albert Ko for supervising me in Salvador. Thank you to Harvey Weinstein for mentoring my throughout my research experience in the Joint Medical Program, and thanks to Art Reingold for serving on my committee and for providing me with valuable feedback.

Urban Leptospirosis in Salvador, Brazil: A Case-Control Study to Identify Risk Factors for Disease Acquisition During an Epidemic

Introduction

Leptospirosis is a zoonosis of worldwide distribution. It is caused by a spirochete that is usually transmitted to humans through contact with the urine of infected animals. The spectrum of disease can range from a mild, subclinical infection to a severe syndrome of multi-organ failure with high mortality[1]. Traditionally a rural- and occupation-based disease, leptospirosis has emerged as a cause of epidemics associated with high mortality among the urban poor in developing countries[2-5].

Between 1987 and 1999, 39,296 leptospirosis cases were reported in Brazil, with an average case fatality ratio of 10.6%, corresponding to 4,159 deaths[6]. These cases represent only the severe, hospitalized cases, as surveillance of leptospirosis occurs only at the hospital level. Because only 5% - 15% of recognized cases are estimated to progress to the severe stage, the number of reported cases represents only a small fraction of the total number of leptospirosis cases in Brazil during this period[7, 8]. Annual epidemics of leptospirosis are associated with periodic flooding that occurs during normal seasonal levels of rainfall, and cases are clustered in low-income areas characterized by open sewers[2, 3, 9]. Although large numbers of people in these areas are exposed to contaminated water, only a small proportion of individuals develop severe leptospirosis, suggesting that specific activities or risk factors are responsible for infection.

A matched case-control study was previously performed in Salvador, Brazil to identify activities in the occupational and residential environments associated with acquisition of leptospirosis[10]. In that study, cases were asked about habitual exposures in interviews that took place 1 – 6 months following the disease episode. In the follow-up study being described here, we also used a matched design, but we interviewed cases an average of 3 weeks following hospital discharge to identify specific activities and exposures in the community during periods of rainfall that might have been associated with leptospirosis. Identification of such community-specific activities is important for guiding future prevention efforts.

Methods

Hospital Based Surveillance For Leptospirosis Cases

An outbreak of leptospirosis was identified in Salvador, Brazil, a city with over 2 million inhabitants, during the rainy season between April and November of 2001. The outbreak was identified through active surveillance at Hospital Couto Maia, the state-run infectious disease reference hospital. State health secretary protocol mandates that all suspected cases of leptospirosis in the metropolitan region of Salvador be referred to this hospital. The surveillance case definition used to identify patients was based on presence of all of the following clinical findings characteristic of pate-phase leptospirosis: conjunctival suffusion, jaundice, and acute renal failure (oliguria [urine output <500mL/24 hrs], serum creatinine >2.0 μg/dL, or blood urea nitrogen >150 mg/dL[3]). Patients who had radiological or laboratory evidence for another disease during hospitalization, or who had a discharge diagnosis other than leptospirosis, were excluded from the study. Demographic data, clinical history, and laboratory findings were obtained through interview and medical chart review for all patients meeting the surveillance criteria. Cases for the case-control study were selected from patients hospitalized between April 29th and November 4th 2001, who met the surveillance definition of leptospirosis, were greater than 12 years of age, and had a positive anti-leptospiral IgM ELISA reaction in one or more serum samples.

Selection of Control Individuals

Residential addresses were used to locate the households of index cases and interviews were performed in their homes. Two age and sex-matched controls were identified in the same neighborhood as each case. Ages of control subjects were matched to within 5 years of case ages. The field team surveyed households a distance of 5 domiciles from the index case household and at every household thereafter until an appropriate age and sex-matched control subject could be identified. A second control subject was identified in a similar manner, starting 5 domiciles from the household of the first control subject. The first control subjects were located an average of 8 houses domiciles (35 meters) from the case residence and the second control residence was an average of 16 domiciles (75 meters) from the case residence. Controls were defined as individuals of the same sex and within the same age quartile as the case who had not had a febrile illness in the past month, had not received a diagnosis of leptospirosis in the past year, and were not pregnant.

Data Collection and Definitions

A standardized questionnaire was administered during interviews performed between May and November 2001. Case patients were contacted via telephone and an appointment was made for the interview as soon as possible following hospital discharge. Cases were interviewed a mean of 21 days following hospital admission. Cases were asked about specific activities they engaged in during the two weeks preceding the onset of symptoms, a time period approximating the incubation period of leptospirosis[8]. Controls were prompted to recall their activities during the same period using a reference date.

The questionnaire solicited demographic information, residential sanitary conditions, exposure to potential sources of environmental contamination, work-related, recreational, and domestic activities, exposure to potential animal reservoirs, alcohol use, and also included a set of standardized observations made by the field team members. The following definitions were used to code responses. "Work" was defined as formal or informal-sector remunerative activity taking place within the previous month. Informal-sector labor consists of temporary, contracted employment that is often irregular. An "open sewer" was defined as a collection or outflow of wastewater with inadequate cement covering. "Proximity to accumulated trash" was defined as continuous presence of household trash within 10 meters of a residence. Visual sighting of rats by study subjects was used to assess presence of rodent reservoirs.

Serologic Case Confirmation

According to the surveillance protocol, paired acute and convalescent-phase serum samples were obtained from suspected patients within 24 hours of admission and at a follow-up outpatient visit after hospital discharge (>14 days after collection of the first sample), respectively. Sampled were tested using the anti-leptospiral IgM enzyme-linked immunosorbent assay (IgM ELISA) according to the method presented by Terpstra et al[11]. A strain of *Leptospira interrogans* serovar copenhageni isolated from a patient in Salvador was used as the antigen source[3]. Cases were defined as confirmed if the absorbance of an acute or convalescent serum was greater than a threshold optical density used to define a positive reaction[12].

A convalescent-phase serum sample was collected at the time of interview from cases that did not previously submit a sample. All cases included in the case-control study had a positive IgM ELISA in either the acute or the convalescent serum sample. The microagglutination test (MAT) was performed as an additional confirmatory test[3]. An MAT-confirmed case exhibited a fourfold rise in agglutination titers between paired samples or a reciprocal titer>800 in at least one sample. Cases were excluded if the case did not have an ELISA confirmed diagnosis. A blood sample was collected from neighborhood controls at the time of interview in order to assess for recent exposure to leptospirosis. Controls with a positive ELISA result were excluded.

Statistical analysis

EpiInfo (6.04) software was used for data entry and analysis of hospital-based surveillance and the case-control study. ANOVA and the X^2 test were used to compare means and proportions, respectively. The association between risk factors and leptospirosis was assessed by both univariate and multivariate analysis. For the univariate analysis, continuous variables were dichotomized at the median value. Mantel-Haenzel odds ratios (OR) for matched data and summary X^2 with the McNemar correction were used to assess associations. The multivariate analysis combined highly correlated covariates, such as work-related and domiciliary exposures to environmental sources of contamination, into a single variable. A backward-elimination method was used to test all variables in a conditional logistic regression model. Multivariate analysis was performed on Intercooled STATA 6.0.

Results

Outbreak Investigation

The outbreak corresponded with an increase in monthly rainfall, a phenomenon that has been reported in previous studies[1,3] (Figure 1).

There were 108 hospitalized cases of leptospirosis that met the surveillance criteria between April 29 and November 4, 2001 (Table 1). Of these cases, 9 (8%) died during hospitalization and 62 (65%) participated in the case-control study. Thirty-seven cases (26%) could not be located following hospital discharge. The cases included in the study did not significantly differ from the total number of hospitalized cases in terms of age, sex, days hospitalized, rate of jaundice, and rate of fever. The incidence of severe leptospirosis for Salvador (population 2, 211,539) was 4.3 per 100,000 persons during the study period.

Demographic characteristics

One hundred and twenty-four control individuals matched by age, sex, and neighborhood of residence were interviewed.

Table 2 summarizes selected findings of the matched univariate analyses for risk factors associated with the acquisition of leptospirosis. The average age of study participants was 33.2 years and 83% were males. The average income of the head of a subset of households did not significantly differ between cases (mean 110 US$) and controls (mean 114 US$; p=0.188). The average number of people living in case and control homes was 5, and the average number of years of residence at the current location was 17 in both cases and controls. Both cases and controls lived in unregistered housing at high rates (43% and 26%). Cases were more likely than controls top be illiterate, however (11% vs. 3%; matched OR 4.33; 95% CI, 0.94 – 25.63), though this was not a statistically significant association. Drinking alcohol every day of the week was associated with leptospirosis (matched OR 4.00; 95%CI 0.85 – 24.72), but again this was not a statistically significant association.

Environmental exposures

Cases and controls each were exposed to rainwater, sewer, mud, and trash at high frequencies (83% and 48%). Cases, however, reported significantly higher rates of each individual exposure (Table 1). Cases also were more likely than controls to spend at least 6 hours per day outdoors (matched OR 2.44; 95%CI: 0.94 – 6.33). Leptospirosis was not associated with type or absence of footwear, however. Exposures occurred in both residential and occupational environments. Thirty-two of the 62 cases (51%) reported exposures occurring both at home and at work, while 25% reported exposures only at home and 25% reported exposures only at work.

Residential exposures

Exposure to environmental sources of contamination in the domiciliary environment was associated with leptospirosis. Cases were significantly more likely than controls to report exposure to rainwater, sewage, mud, and trash at home (Table 2). Sewage systems in which wastewater from the house went into an open sewer were more frequent among cases than controls (matched OR 2.86; 95%CI 0.93 – 8.07), although the difference was not statistically significant. Municipal trash collection was not associated with leptospirosis, as trash was not collected from 37% of case households and 30% of control households.

Occupational exposures

Occupational exposure to contaminated sources was also associated with leptospirosis. Cases were significantly more likely than controls to report exposure to rainwater, sewage, mud, and trash at work (Table 2). Cases were more likely to be employed (matched OR 2.36; 95%CI 1.06 – 5.50), to work at least 40 hours per week (matched OR 3.27; 95%CI 1.39 – 7.53), and to work outdoors (matched OR 3.42; 95%CI 1.57 – 7.86). Employment in the informal labor sector only was significantly associated with leptospirosis when all of the cases were compared to controls (matched OR 2.31; 95%CI 1.15 – 4.67) but not when only those cases and controls that were employed were compared (matched OR 2.23; 95%CI 0.88 – 6.12). Work with sewers (matched OR 11.00; 95%CI 1.24 – 492.75), work in construction (matched OR 4.17; 95%CI 1.38 – 12.52), and working in proximity to a storage area (matched OR 2.42; 95%CI 1.05 – 6.33) were specific occupational variables associated with leptospirosis.

Rat sightings

Both cases and controls lived in rat-infested environments, as 84% and 76%, respectively, reported regular rat sightings. Rat sightings during the daylight hours, however, were associated with leptospirosis (matched OR 2.22; 95%CI 1.14 – 4.34). Sighting more than 5 rats in the domiciliary yard (matched OR 3.20; 95%CI 0.90 – 11.94) and occupational rat sightings (matched OR 2.64; 95%CI 1.09 – 6.07) were also reported by cases with greater frequency. Leptospirosis was associated with the presence of an empty lot adjacent to the domicile (matched OR 1.84; 95%CI 0.91 – 4.20). Cat ownership was found to have a protective effect (matched OR 0.36; 95%CI 0.14 – 0.95), while presence of dogs and chickens had no discernable effect.

Duration of Exposure

Increased duration of exposure was found to be associated with leptospirosis in the univariate matched analysis. Contact with rainwater for periods of greater than one hour was significantly more common among cases, as were exposures to sewage and mud of greater than 5 minutes (Table 2).

Multivariate Analysis

Table 3 summarizes the results of the conditional logistic regression model. Workplace exposure to sewage and mud was independently associated with acquisition of leptospirosis (matched OR 3.67; 95%CI 1.51 – 8.95). Residential contact with sewage, mud, and trash (matched OR 1.74; 95%CI 1.03 – 2.93) was also found to be associated with infection. Sighting 5 or more rats (matched OR 2.33; 95%CI 0.95 – 5.76) was a third variable that was found to be associated with leptospirosis, but this association was not statistically significant.

Home vs. work comparison of exposures

Cases were asked about specific activities that they believed might have led to infection. Cases were separated into three distinct groups according to reported site of exposure: residential exposures only, occupational exposures only, and both types of exposures. Fifteen cases reported only occupational exposures, 15 reported only residential exposures, and 32 reported mixed exposures. Specific activities reported among work-related exposures included digging (4 cases, 27%), stepping in mud or water (3 cases, 20%), handling construction material (2 cases, 13%), and clearing a sewer (1 case, 7%). Three (20%) cases reported spending extended periods of time in rat-infested areas. Among residential exposures, activities reported included stepping in water or mud (5 cases, 33%), cleaning the yard (4 cases, 27%), gathering trash (2 cases, 13%), flooding in the house (1 case, 7%), and falling into a sewer (1 case, 7%). All of the cases reporting work related exposures only were males, while 9 (60%) of the cases reporting residential exposures only were males (Fisher's exact test p = 0.017). The mean ages were 27 in the work exposure group and 34 in the residential exposure group.

Discussion

A previous community-bases case-control study identified residence in proximity to an open sewer, residential sighting of rats, sighing of groups of 5 or more rats, and workplace exposure to contaminated environmental sources to be associated with clinical leptospirosis. This current study found similar associations, particularly the association of leptospirosis with both residential and occupational exposures, as well as the sighting of rats. In addition, however, we found duration of exposure to be associated with infection. In particular, the gender difference in cases reporting occupational exposure versus residential exposure has not been previously identified in this setting. Because the interviews in this study were conducted soon (average of 3 weeks) after discharge of a case, we were able to obtain information that may not have been possible to obtain accurately in the previous study.

In this study, the occupational exposure was the strongest association (matched OR 3.67). Leptospirosis has long been considered an occupational disease[1, 13], especially in rural environments In this epidemic, residential exposure was also associated with disease, however (matched OR 1.74). This supports the notion that leptospirosis cannot be considered a disease associated exclusively with high-risk occupations in urban settings such as Salvador. This represents a new epidemiologic pattern of leptospirosis: annual urban epidemics associated with seasonal rainfall.

Traditionally, the observed gender difference in clinically overt leptospirosis, where male-to-female ratio is nearly 3:1, has been attributed to occupational exposure differences. Our findings seem to support this suggestion, even in the urban setting. When we separated cases based on exposure site, we found that while 100% of the cases that reported only occupational exposure were male, 60% of those reporting residential exposure were male and 40% were female. Residential exposures are thus more equally shared between the sexes than occupational exposures, indicating that the preponderance of male cases in a leptospirosis epidemic may be due to exposure differences rather than biological or immunological factors.

The study was limited by the case-selection design based on hospitalized cases of severe leptospirosis. Since severe cases represent only about 5-15% of all cases[7, 8], the majority of leptospirosis cases in Salvador were not likely to be hospitalized and thus were not included in the study. Furthermore, 35% of the hospitalized cases were not interviewed due to death or our inability to locate them following discharge. To compensate for the small sample size, two controls were selected for each case. Matching according to neighborhood and sex may have inadvertently masked other risk factors, and as in all case-control studies, ability to recall exposures may have differed between cases and controls. Nevertheless, we were able to identify significant differences in exposures by residents sharing very similar conditions within their community.

Conclusion

Leptospirosis epidemics have been occurring in urban Brazil and Latin America for the past 40 years[4, 14-16]. This time period has coincided with a 350% increase in the urban population of Brazil and the creation of urban slums lacking basic sanitation[17]. This study shows that, in this type of urban environment, specific exposures occur in the residential as well as the occupational environment, and that exposures are common and associated a diverse range of activities. In the residential environment, females are just as susceptible to infection and likely to develop disease as males. However, despite widespread environmental contamination in neighborhoods of cases and controls, there appear to be differences that determine the development of disease in a select few. These may include inoculum dose differences, baseline immunity, or other unrecognized factors.

Early diagnosis of leptospirosis is difficult due to its nonspecific initial clinical presentation[18]. The mortality rate of advanced, hospitalized cases in this epidemic was 8% and has been reported to be as high as 50% in Rio de Janeiro and Sao Paolo[19, 20]. Prevention is thus the key to decreasing mortality and hospitalization. Prevention efforts must be made at multiple levels. The findings from this type of study may be incorporated into improved intervention strategies at the community level.

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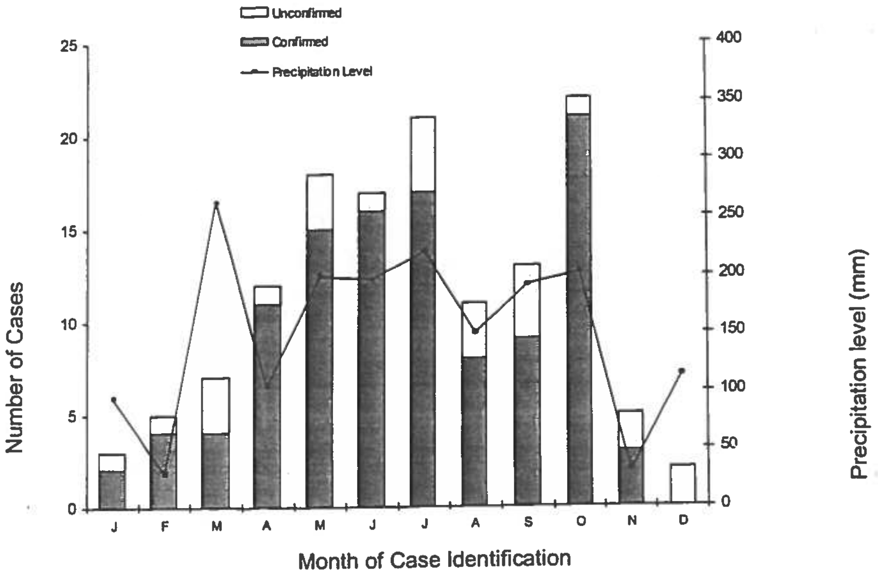
Figure 1.

Monthly Distribution of Severe Leptospirosis Cases in Salvador, 2001



Confirmed cases were confirmed using IgM ELISA and MAT. Unconfirmed were diagnosed clinically or had one serum positive in IgM ELISA or MAT.

Table 1. Case Characteristics

Characteristic	Cases Included in Study n = 62	All Hospitalized Cases n = 108	Deaths n = 9
Median Age	33 (14 – 63)	34 (9 - 63)	45 (29 - 63)
Male	52 (83%)	90 (83%)	8 (89%)
Median Days Hospitalized	6 (2-15)	6 (1-30)	4 (0-9)
Jaundice	47 (77%)	80 (74%	9 (100%)
Fever	57 (93%)	101 (93%)	9 (100%)

Table 2 Univariate Matched Analysis of Risk Factors for Acquisition of Leptospirosis

Variable	N	Cases No. (%)	N	Control Subjects No. (%)	OR (95% CI)	P-value
Demographic						
Illiterate	62	7 (11)	124	4 (3)	4.33 (0.94 – 25.63)	0.057
House is not officially registered	62	21 (34)	123	32 (26)	1.67 (0.72 – 3.90)	0.264
Average # years living in current home	62	16.5	124	16.8	-	0.838
Income of head of household	39	270.9	78	280	-	0.188
Average # of people living in house	62	5.2	124	5.3	-	0.194
Drinks 7 days of the week	62	12 (19)	124	15 (12)	4.00 (0.85 – 24.72)	0.077
Exposure to contaminated sources						
Contact with rainwater	61	37 (61)	122	44 (36)	3.58 (1.54 – 7.43)	0.001
Contact with sewage	60	24 (40)	120	15 (12)	5.86 (2.44 – 19.09)	0.000
Contact with mud	61	23 (38)	121	16 (13)	4.00 (1.80 – 8.80)	0.000
Contact with trash	60	27 (45)	119	19 (16)	4.40 (2.00 – 9.60)	0.000
In open air > 6 hrs/day	39	32 (82)	78	51 (65)	2.44 (0.94 – 6.33)	0.076
Wearing boots	39	4 (10)	78	2 (3)	4.00 (0.73 – 21.84)	0.194

Wearing only sandals	39	19 (50)	78	26 (33)	2.50 (0.84 – 6.32)	0.122
Barefoot	39	4 (10)	78	8 (10)	1.00 (0.28 – 3.61)	0.737
Exposure to contaminated sources in the residential environment						
Contact with rainwater at home	61	14 (23)	122	20 (16)	1.73 (0.65 – 4.28)	0.338
Contact with sewage at home	60	12 (20)	120	8 (7)	6.33 (1.52 – 33.87)	0.006
Contact with mud at home	61	9 (15)	122	7 (6)	2.83 (0.87 – 9.61)	0.083
Contact with trash at home	60	12 (20)	120	10 (8)	2.75 (1.10 – 6.89)	0.048
Wastewater goes into open sewer	62	32 (52)	124	51 (41)	2.86 (0.93 – 8.07)	0.069
Open sewer w/in 10 meters	62	23 (37)	124	36 (29)	1.53 (0.72 – 3.60)	0.288
No trash pickup	62	23 (37)	121	36 (30)	2.25 (0.81 – 6.22)	0.168
Exposure to contaminated sources in the occupational environment						
Contact with rainwater at work	61	13 (21)	122	8 (7)	3.25 (1.25 – 9.05)	0.011
Contact with sewage at work	60	9 (15)	120	2 (2)	9.00 (1.86 – 85.60)	0.002
Contact with mud at work	61	10 (16)	122	4 (3)	6.33 (1.68 – 23.50)	0.004
Contact with trash at work	60	12 (20)	120	2 (2)	12 (2.69 – 53.62)	0.000

If employed, only informal	45	30 (67)	72	36 (50)	2.23 (0.88 – 6.12)	0.098
Works @ least 40 hrs/week	62	36 (58)	124	47 (38)	3.27 (1.39 – 7.53)	0.004
Works at all	62	46 (74)	124	73 (59)	2.36 (1.06 – 5.50)	0.036
Works with sewer	62	6 (10)	124	2 (2)	11.0 (1.24 – 492.75)	0.023
Works in construction	62	15 (24)	124	11 (9)	4.17 (1.38 – 12.52)	0.007
Street peddler	62	4 (7)	124	8 (7)	1.00 (0.19 – 4.45)	0.737
Ever works in open air	62	36 (58)	124	44 (36)	2.87 (1.41 – 6.57)	0.003
Reservoirs						
Sees rats anywhere	62	53 (86)	124	94 (76)	2.00 (0.84 – 4.78)	0.175
Sees rats @ work	62	17 (27)	124	16 (13)	2.64 (1.09 – 6.07)	0.027
Sees rats in the quintal	62	23 (37)	124	39 (32)	1.27 (0.64 – 2.55)	0.553
Sees >5 rats in the quintal	62	9 (15)	124	7 (6)	3.20 (0.90 – 11.94)	0.073
Sees rats during the day	62	40 (65)	124	58 (47)	2.22 (1.14 – 4.34)	0.027
Empty lot adjacent to home	61	28 (46)	122	39 (30)	1.90 (1.00 – 3.90)	0.070
Owns cat	62	5 (8)	124	26 (21)	0.36 (0.14 – 0.95)	0.040
City placed poison/traps	61	20 (33)	120	44 (37)	0.83 (0.39 – 1.74)	0.755

Duration of Exposure						
Contact with rainwater for > 1 hour	61	18 (30)	124	15 (12)	3.44 (1.41 – 9.54)	0.004
Contact with sewage for > 5 minutes	60	15 (25)	124	10 (8)	4.33 (1.50 – 13.53)	0.003
Contact with mud for > 5 minutes	61	17 (28)	124	9 (7)	5.33 (1.94 – 16.25)	0.000

Table 3. Multivariate Analysis of Risk Factors: Results of conditional logistic regression with matched data, adjusting for other risk factors in the model

	Cases	Control	Adjusted OR	(95% CI)	P-value
	(n=60)	(n=120)			
Residential contact with sewer, mud, trash	20 (33)	19 (16)	1.74	1.03 - 2.93	0.039
	(n=61)	(n=122)			
Workplace exposure to sewer or mud	14 (23)	4 (3)	3.67	1.51 – 8.95	0.004
	(n=62)	(n=124)			
Sighting groups of 5 or more rats	19 (32)	16 (13)	2.33	0.95 - 5.76	0.065

Transition

While the results of the case-control study have important implications, there are some important limitations associated with the findings. These limitations are addressed in the following paper. A meta-evaluation of the social epidemiological literature critiquing methods that focus on individual-level risk factors is presented in order to frame the issues in the broader context of current epidemiological research theory.

An Evaluation of the Case-Control Method and a Meta-evaluation of the Limits of Epidemiology

Introduction

The explosion of the AIDS pandemic in the 1980s and 90s has ushered in a new era in public health. HIV/AIDS is the most prominent member of the recently characterized group of "emerging and re-emerging infectious diseases". These have been defined as "infections that have newly appeared in a population or have existed but are rapidly increasing in incidence or geographic range"[1]. The factors responsible for the emergence of these diseases have been identified by the Institute of Medicine and the Centers for Disease Control and Prevention as ecologic changes and agricultural development, human demographics and behavior, international travel and commerce, technology and industry, microbial adaptation and change, and the breakdown in public health measures[1-3]. David Satcher, as head of the CDC, placed the responsibility for addressing the new challenge posed by emerging infections on "the custodians of public health", invoking the maxim: "the health of the individual is best assured by maintaining or improving the health of the entire community"[4]. Satcher particularly emphasized the role of behavioral science, pointing out that "having the science or laboratory technology to control infectious disease is not enough unless we can influence people to behave in ways that minimize the transmission of infections and maximize the efforts of medical interventions"[4]. He proceeded to call for interdisciplinary collaboration between microbiologists, infectious disease specialists, and basic, clinical, and behavioral scientists in the effort to control and prevent infectious disease.

Leptospirosis has been identified by the Institute of Medicine as one of the re-emerging infectious diseases[3]. The objective of this paper is to use a recently completed case-control study of leptospirosis to explore the strengths and limitations inherent in contemporary epidemiological research, and to propose new directions of inquiry that address some of these limitations. A meta-evaluation of the social epidemiological literature critiquing contemporary epidemiological approaches will be presented in order to frame the issues.

The primary limitations of the case-control model that I identify are an overly individualistic framework and the absence of a socio-historical context. The findings of the meta-evaluation show that these limitations have been identified by epidemiologists in various contexts and indicate a need to broaden the analytical perspective of epidemiology. Many researchers call for an ecological perspective that addresses interconnections between individual and biological, physical, social, and historical contexts and that integrates macro- and microlevels of analysis. This perspective is employed by medical anthropologists who study health and illness, pointing to a potentially fruitful area of cross-disciplinary collaboration. In this paper, I propose a framework for studying leptospirosis that integrates epidemiological and anthropological perspectives.

Case Study: Leptospirosis in Brazil

Leptospirosis is a zoonosis of ubiquitous worldwide distribution, but it is most common in tropical environments[5,6]. It is caused by a spirochete that is usually transmitted to humans through contact with the urine of infected animals. The spectrum of disease in humans can range from a mild, asymptomatic infection to a severe syndrome involving multi-organ failure and high mortality[7]. Traditionally, leptospirosis was associated with a rural setting and certain high-risk occupations, such as sewer workers, meat workers, miners, and fishermen[8,9]. Recently, however, leptospirosis has been identified as an important emerging infectious disease of the urban environment,[8-12] associated with rat infestation and poor infrastructure.

Brazil has been undergoing a massive demographic transformation since 1960 that has caused a 350% increase in its urban population[8, 13]. The majority of the migrants to cities are rural poor who reside in ever-expanding urban slums, *favelas*, where the lack of basic sanitation favors rodent-born transmission of leptospirosis[8]. In large Brazilian cities, approximately 3600 patients were hospitalized annually for leptospirosis through the 1990s[14]. Recurrent epidemics of leptospirosis are associated with periods of heavy rainfall and flooding, and cases are predictably clustered in low-income areas characterized by open sewers[8, 15-17]. Descriptive studies characterizing a single outbreak and demonstrating the cyclic nature of the annual leptospirosis epidemics in Salvador, Brazil have previously been carried out[8, 17]. Successive retrospective and prospective matched case-control studies have been designed and performed, with the objective of identifying risk factors associated with acquisition of leptospirosis in Brazil[18, 19]. This analysis focuses on the prospective study[19].

Case-Control Methodology

The objective of the case-control study was to assess the role of various activities and factors at the community level that occurred during the period of exposure. It is prospective because cases were interviewed as soon as they became eligible to participate in the study, during the epidemic. In contrast, the retrospective study examined cases after the epidemic had ended. An outbreak of leptospirosis was identified in Salvador beginning in April of 2001. For the case-control study, cases were selected from among serologically confirmed leptospirosis cases that were hospitalized during the epidemic, which lasted until November, 2001. Cases were located using residential addresses. Two control individuals of the same sex and within 5 years of age of the case were selected from the same neighborhood as the case. The first control individual was located by surveying 5 domiciles from the index case household and at every household thereafter until an appropriately matched individual could be located. The second control individual was located by surveying 5 domiciles beyond the house of the first control subject. A serologic test for evidence of exposure to leptospirosis was performed on blood samples from control individuals, and individuals with a positive serologic test were excluded from the study. A standardized, structured questionnaire was administered during interviews performed at the homes of cases and controls. Cases were asked about specific activities they engaged in during the two weeks preceding the onset of symptoms, a time period approximating the incubation period of leptospirosis[5]. Control individuals were prompted to recall activities during the same period using a reference date. The questionnaire solicited demographic information, residential sanitary conditions, exposure to potential sources of environmental contamination, work-related, recreational, and domestic activities, exposure to potential animal reservoirs, and alcohol use. In addition, the field team members made a set of standardized observations of the house and its surroundings.

ANOVA and the X^2 test were used to compare means and proportions, respectively. The association between risk factors and leptospirosis was assessed by both univariate and multivariate analysis. Mantel-Haenzel odds ratios (OR) for matched data and summary X^2 with the McNemar correction were used to assess associations. The multivariate analysis combined highly correlated covariates, such as work-related and domiciliary exposures to environmental sources of contamination, into a single variable. A backward-elimination method was used to test all variables in a conditional logistic regression model.

Findings of the Case-control Study

This is the first prospective case-control study of urban leptospirosis. It is also the first study to report specific activities associated with leptospirosis during an urban outbreak.

Leptospirosis in Salvador during the epidemic was associated with exposure to contaminated sources, such as floodwater, sewage, mud, and trash, in both residential and occupational settings. These findings suggest a new epidemic pattern in which entire urban neighborhoods are at risk rather than certain occupations or rural areas. In occupational settings, all of the leptospirosis cases are in men. In residential settings, however, 40% of the cases are in women, representing a substantially different sex distribution of the cases. In these domestic settings, cases in women are nearly as frequent as cases in men. This may indicate that the preponderance of male cases reported in the literature is due to the fact that men are exposed more frequently by virtue of their occupations.

The exposures associated with acquisition of leptospirosis in the urban settings in Brazil are common and widespread. Coupled with the difficulty of diagnosing leptospirosis early and the difficulty in treating late-stage severe leptospirosis, these results indicate that prevention efforts at multiple levels are the key to decreasing mortality and hospitalization.

Limitations of the Case-Control Study

While the findings of the case-control study represent important advances in the study of leptospirosis, there are also limitations to the results. The principal limitations of the leptospirosis case-control study include a singular focus on the individual and the absence of a socio-historical context. These features of the study design neglect important behavioral factors affecting disease transmission and may impede our ability to apply the results of our studies to practical public health improvements.

The goal of the study design and subsequent statistical analysis was to distinguish individual risk factors for acquisition of leptospirosis, such as contact with contaminated environmental sources and sighting groups of 5 or more rats at one time. The isolation and separation of the individual from the socio-historical context results in an incomplete picture of disease transmission. The focus is on the host-pathogen interaction, and the objective is to elucidate how and under what circumstances leptospires enter the body of the individual and cause disease. The variables measure behaviors and characteristics of the individual that may put him or her into contact with environmental sources contaminated by bacteria. The nature of this contact is characterized in terms of the location of the exposure, the duration of the exposure, and the specific activity associated with the exposure. The result of such an approach is a framework in which the focus is on biological agents or individual risk factors as contributors to disease while ignoring the characteristics of social organization, economic factors, or specific policy decisions that may be equally or even primarily contributory. While the individual risk factors are important to characterize so as to direct intervention efforts, they lose much of their meaning when removed from their social context.

Understanding patterns of health and behavior requires viewing the patterns as a consequence of social relationships, rather than simply as the sum of individual traits and choices. Epidemic leptospirosis in Salvador, Brazil does not occur only because of individual behaviors, but also as a result of structural, economic, and political factors that lead to the maintenance of basic sanitary and infrastructural deficiencies in the *favelas*. Restricting the focus of the study to individual risk factors ignores the underlying historical and social influences on individual behavior and may even serve to obscure the true cause of disease. At worst, such a perspective may mistakenly make the individual appear culpable or responsible for the infection. Focusing on the individual while ignoring the structural causes of disease ignores overarching issues of social justice and equity.

The complex historical and social context of urban Brazil that shapes the lives of those at risk for leptospirosis is not reflected in the case-control study design. While all of the published studies of epidemic leptospirosis in Salvador have acknowledged the fundamental role played by poverty in disease transmission, poverty and inequality are treated as variables in the case-control study, on a par with other variables such as having had contact with rainwater, sewage, or mud. While a picture of urban poverty emerges from variables such as "percentage of houses serviced by open sewer", "sighting of rats during the day", "no trash pick-up", and "illiteracy", the picture is incomplete because it is not grounded in any sort of social or historical context.

We have a picture of the behaviors and the conditions that lead to exposure, but it is largely a two-dimensional picture. We do not see why the conditions exist, and a realistic way of addressing the conditions does not emerge. We also have little insight into individual behavior and what shapes it. We neither see if the behaviors that lead to exposure are modifiable, nor do we understand why individuals choose to engage in such behaviors. There may be gender specific exposures occurring as a consequence of distinct social roles and behavior patterns. This information does not emerge from individual-level data. Without this information, we may not completely understand the dynamics of disease transmission and are not equipped to design successful interventions. Epidemiologist AJ McMichael's criticism that modern epidemiology "is oriented to explaining and quantifying the bobbing of corks on the surface waters while largely disregarding the stronger undercurrents that determine where, on average, the cluster of corks ends up along the shoreline of risk"[20] rings particularly true in this instance. The individual risk factors for disease acquisition that we have documented only hint at the underlying socioeconomic factors that lead to leptospirosis epidemics.

Meta-evaluation

In order to illustrate that the limitation of this case control study discussed above is characteristic of epidemiological studies in diverse contexts, a meta-evaluation of the social epidemiologic literature critiquing an approaches based on characterization of risk factors is presented.

Meta-evaluation Methods

The meta-evaluation of social epidemiological literature includes papers that discuss the limitations of current methods in epidemiology, referred to as "modern" or "risk factor" epidemiology and also proposes new frameworks of analysis that attempt to address the identified limitations. The papers are all reviews and editorials rather than studies presenting primary research findings and were all published between 1994 and 2002. A literature search using the key words epidemiology/trends, social environment, and public health/health care science was conducted on PubMed. Bibliographies of papers were also searched by hand and one paper that was not indexed on PubMed was located using this method and included in the meta-evaluation. I sought papers proposing frameworks that accounted for the factors that I found to be missing from the leptospirosis case-control study discussed above. The key words selected to conduct the search were intended to identify works that addressed these issues. Because the factors are social in nature, I focused on the social epidemiological literature. The literature reviewed here is not meant to be all-inclusive, but rather representative of some of the predominant themes within the field.

Meta-evaluation Results

The nine papers that were selected are summarized in the following table:

Selected Critiques of Modern Epidemiology				
authors	**title**	**year**	**critique**	**proposal**
N. Krieger	Theories for Social Epidemiology in the 21st	2001	Psychosocial theory in social epidemiology directs attention to endogenous biological	Ecosocial theory and related multi-level dynamic perspectives that ask

	Century: An Ecosocial Perspective		responses to human actions but pays less attention to who and what generates psychosocial insults and buffers and how social, economic, and political policies shape their distribution. The social production of disease perspective does not offer principles for thinking through which specific public health and policy interventions are needed to curtail social inequalities in health.	"who and what drives current and changing patterns of social inequalities in health, embracing a social production of disease perspective while aiming to bring in a rich biological and ecological analysis
S. Schwartz, E. Susser, and M. Susser	A Future for Epidemiology?	1999	The current risk factor paradigm disproportionately concentrates on the description of risk factor/disease relationships rather than on the explanation of causal processes and is preoccupied with the individual level of organization to the exclusion of other levels.	An eco-epidemiology that addresses the interdependence of individuals and their connection with the biological, physical, social, and historical contexts in which they live.
AJ McMichael	Prisoners of the Proximate: Loosening the Constraints on Epidemiology in an Age of Change	1999	The following four constraints of modern epidemiology limit the engagement of issues in wider context: 1) a preoccupation with proximate risk factors; 2) a focus on individual-level versus population-level influences on health; 3) a modular, life-	Epidemiologists must broaden their causal models and recognize the important ecologic dimensions of social-environmental influenceson health and disease; epidemiology must integrate across

			stage view of how individuals undergo changes in risk status; 4) the challenge of forecasting of health consequences of future, large-scale social and environmental changes.	macro-, meso-, and microlevels of causal analysis and deal with complex social and ecologic relations.
M Susser and E Susser	Choosing a Future for Epidemiology: I. Eras and Paradigms, II. From Black-Box to Chinese Boxes and Eco-Epidemiology	1996	A focus on individual risk factors ignores important information about the social context of disease transmission and illness.	A localizing ecological paradigm that is equally concerned with causal pathways at the societal level and with pathogenesis and causality at the molecular level.
N Pearce	Traditional Epidemiology, Modern Epidemiology, and Public Health	1996	Epidemiology has shifted its level of analysis from the population to the individual and has become a set of generic methods for measuring associations of exposure and disease in individuals.	Epidemiology must reintegrate itself into public health and must rediscover the population perspective.
B.G. Link and J.C. Phelan	Social Conditions as Fundamental Causes of Disease	1995	Question the focus on individually-based risk factors and argue that greater attention be paid to basic social conditions.	Individually-based risk factors must be contextualized by examining what puts people at risk of risks and social factors such as SES and social support are likely "fundamental causes" of disease.
S Wing	Limits of Epidemiology	1994	Epidemiology's contribution to public health is constrained by a preoccupation with universal exposure – disease	Exposure – disease studies can be integrated into a broader public health perspective in which specific

			relationships that impedes consideration of the contexts in which exposures occur; public health interventions narrowly focused on exposure-disease relationships cannot address the more important public health effects of the industries and social arrangements that produce exposures studied by epidemiologists.	exposures are considered as agents acting in a context rather than as autonomous causes of disease; epidemiology can improve its contribution to public health and achieve a far greater level of social responsibility by recognizing the historical contexts of public health phenomena and the sciences that address them.
N. Krieger	Epidemiology and the Web of Causation: Has Anyone Seen the Spider?	1994	The multiple causation framework dominant in modern epidemiology does not address the origins of the multiple causes. It emphasizes biological determinants of disease amenable to intervention though the health care system, considers social determinants of disease to be secondary, and reduces disease in populations to a question of disease in individuals.	An ecosocial epidemiologic theory that embraces population-level thinking and rejects the underlying assumptions of biomedical individualism, integrating social and biological understandings of health, disease, and well-being.

The papers included in the meta-evaluation question the focus on individual-level risk factors in modern epidemiology. Krieger points out that by relying on an underlying theoretical framework of biomedical individualism, "disease in populations is reduced to a question of disease in individuals, which in turn is reduced to a question of biological malfunctioning. The biologic substrate, divorced from its social context, thus becomes the optimum locale for interventions, which are chiefly medical in nature"[21]. Addressing the overall epidemiological approach, Krieger maintains that the focus upon the individual as the unit of study limits the scope of inquiry. Krieger's criticism applies to the case-control study of leptospirosis.

The result of such an approach is a list of risk factors that Wing characterizes as "a kind of human toxicology" in which "it is only agents or risk factors, not characteristics of the organization of populations, that are eligible to be causes of disease"[22]. It misses the important dynamics affecting disease transmission that may not be occurring on the individual level and thus cannot be measured or observed by focusing on the individual. As Susser and Susser point out with reference to HIV, "analysis of mass data at the individual level of organization alone....does not allow us to weigh at which points in the hierarchy of levels intervention is likely to be successful"[23].

Pearce outlines the historical move that epidemiology has made in shifting its level of analysis from the population to the individual, becoming a set of generic methods for measuring associations of exposure and disease while ignoring the greater context[24]. Wing contends that a consideration of the context in which exposures occur is impeded by a preoccupation within epidemiology of universal exposure-disease relationships[22]. Lack of knowledge regarding the sociocultural context represents an important gap in our understanding of leptospirosis and this gap may exist in our understanding of other diseases as well.

McMichael identifies four constraints of modern epidemiology that limit the engagement of issues in a wider context: a preoccupation with proximate risk factors, a focus on individual-level versus population-level influences on health, a modular view of how individuals undergo changes in risk status (life-stage versus life-course), and the challenge of forecasting of health consequences of future, large-scale social and environmental changes[25]. McMichael echoes the criticisms of his colleagues in outlining the limits of risk-factor epidemiology.

The findings of the meta-evaluation outlined above suggest gaps in the research and point to new directions of study. The authors propose new frameworks for studying patterns of disease distribution that embrace population-level thinking, explicitly reject an individualistic framework, and incorporate multi-level frameworks of analysis. In proposing an alternative to risk-factor epidemiology, Susser and Susser propose a "localizing ecological paradigm" that is equally concerned with "causal pathways at the societal level and with pathogenesis and causality at the molecular level"[26]. They propose an expansion of the traditional epidemiologic model to include causal thinking at several levels of analysis: the molecular level, the individual - behavioral level, the population level, and the global level. This approach could be applied to study epidemic leptospirosis. On a molecular level, the precise means of transmission of leptospirosis is important to characterize, as is the identification and differentiation of the various pathogenic serotypes. On an individual level, the behaviors that lead to infection should be elucidated. At the population level, the dynamics of the epidemic are shaped by societal characteristics such as employment levels, gender roles, household dynamics and characteristics, physical characteristics such as type of sanitation, and housing, ecological characteristics such as proximity to rodent reservoirs, rodent density, and frequency of trash collection.

At the global level, interconnections between societies affect the epidemics in important ways. It is interesting to note that the principal rodent reservoirs of leptospirosis in Salvador, *Rattus rattus* and *R. norvegicus*[8] are likely to have come to South America from Europe on ships during the nineteenth century[27], thus implicating international commerce in the origins of the epidemic. However, more proximate connections between the international community and urban leptospirosis epidemics can be made. Brazil has enthusiastically embraced the development model of the International Monetary Fund and the World Bank, cutting back on public investments in public health and sanitation[28, 29]. These policies have helped create the conditions that lead to transmission of leptospirosis in urban Brazil. Current research on leptospirosis has a heavy slant towards the molecular and individual-behavioral level. Analytic perspectives that address the population and the global level are needed.

Fee and Krieger call for a perspective that asks how individuals' membership in a social group shapes their particular health status, and how their health status reflects their position within society's larger social structure[30]. Krieger points out that changing these population patterns "requires explicitly addressing their political, economic, and ideologic determinants. According to this view, social inequalities in health are the defining problem of the discipline of epidemiology. The litmus test of any epidemiologic theory of causation thus is whether it can explain past and present social inequalities in health"[21]. Krieger proposes the development of an ecosocial framework. Such a perspective moves beyond the narrow focus on individual risk and would enrich and inform the study of epidemic leptospirosis in Brazil, a disease that affects certain economically and geographically defined social groups and is a result of inequality. This perspective would put the isolated risk factors of the case-control study into a context, addressing not only the individual behaviors and characteristics of the physical environment that lead to infection, but also linking these risk factors to social inequality and to the structural processes that create the inequality.

In a recent article discussing theory in social epidemiology, Krieger outlines the limitations of frameworks with a restricted perspective[31]. She points out that even within social epidemiology, psychosocial theory focuses on endogenous biological responses to human interactions without analyzing who and what generates the psychosocial insults and buffers. A social production of disease perspective, on the other hand, does not offer methods of considering specific public health and policy interventions needed to reduce social inequalities in health. An "either/or" perspective is inherently limited. A multilevel research perspective that aims to integrate both a social production of disease perspective and a biological and ecological analysis would yield a more cohesive and rich picture of the dynamic of disease in a population.

Wing proposes an alternative framework that includes the utilization of "historical information, the developmental narratives of particular populations and even individual people, with the aim of connecting the particular and the general. Epidemiology can dramatically improve its contribution to public health and achieve a far greater level of social responsibility by recognizing the historical contexts of public health phenomena and the sciences that address them"[22]. Though Wing does not term the model "ecological", he joins the epidemiologists that I have cited above in calling for an expansion of the scope of epidemiology to include the socio-historical context. In advocating for the use of narratives and connecting the particular to the general, Wing points to the need to examine the dynamics that shape individual risk. Using narratives of people directly affected by the disease would provide a context for their behavior and answer the important question of why people do what they do that puts them at risk. Narrative analysis, however, is a method used by disciplines, such as medical anthropology, outside of the traditional scope of epidemiology.

Towards an Interdisciplinary Collaboration

Scholars in both epidemiology and anthropology have published numerous anthologies and articles exploring the common ground shared by medical anthropology and epidemiology and the potential for collaboration[32-43]. This literature is particularly rich in the area of infectious disease research. The affinity is evident in the model of disease ecology of Brown, Inhorn, and Smith, which includes "at least three levels of causation: (1) a microbiological level, in which agents of disease act within the human body; (2) a cultural ecological (or microsociological) level, in which individual behaviors, encouraged or constrained by sociocultural context, put people at risk for contracting particular diseases; and (3) a political ecological (or macrosociological) level, in which historical factors involving interactions between human groups share people's (often differential) access to resources and their relationship to the physical environment"[44]. This approach is remarkably similar to the ecological approaches espoused by social epidemiologists. This similarity points to a natural area of interdisciplinary collaboration. The key difference is the emphasis on sociocultural variables and the political ecological level of analysis, two perspectives that are missing from the traditional epidemiologic model.

The hallmark of anthropology is the holistic perspective. Anthropologists tend to collect a great deal of information about the economy, societal relations, cultural beliefs, political dynamics, and other features of a community, even when the research is focused on a specific health question[45]. Thus, one of the explicit goals of anthropological research is to offer a context for individual-level data. Anthropologists aim not only to understand individual risk behaviors in a sociocultural context, but also to elucidate the political-economic and ideological factors that give legitimacy to and facilitate the behaviors. These studies "make sense" of individual behavior in the broader social, cultural, and historical context[38]. Anthropologists primarily rely on ethnographic research methods, such as in-depth interviews, participant-observation, and surveys, and often combine quantitative and qualitative data. By establishing long-term, personal relationships with the communities they study, anthropologists record the details of everyday life and family dynamics, elicit local attitudes, beliefs, and values, and pay particular attention to the larger socioeconomic forces that affect the community. The rich picture that emerges would provide epidemiologic data much of the context they lack.

A Qualitative / Quantitative Community Study of Leptospirosis

An ecological model that may be useful to adapt to the study of leptospirosis is provided by Coreil, Whiteford, and Salazar in their study of the household ecology of dengue fever in the Dominican Republic[46]. Their study examined risk behaviors that favored the breeding of mosquitoes in domestic spaces, transmission behaviors that brought mosquitoes into contact with people, and protective behaviors that either decreased mosquito density or reduced exposure of individuals to mosquito bites. Ethnographic and survey methods were used to address these objectives. This model could be adapted to leptospirosis. Though the research design focuses on risk factors and thus potentially may have the same narrow scope as the traditional case-control study, the ethnographic approach allows for the incorporation of the historical context and the narrative of members of the affected communities. Such a study would focus on both the household and the workplace ecology of leptospirosis. It would examine the risk behaviors and the features of the physical environment that bring people into contact with contaminated sources, and that are conducive to maintenance of rodent populations, as well as the protective behaviors that decrease contact with contaminated sources. Official documents and the scientific literature would initially be reviewed to determine past policies and programs relating to rodent control, trash collection, and sanitation in the affected areas and to identify previous ethnographic and community-based research on leptospirosis. Initial data collection protocols would be designed using this information. Community and household areas would then be mapped to establish geographic and environmental parameters of the neighborhood, to map private and public spaces of activity, to identify spatial domains of both the household and of the workplace, and to identify and determine areas with rodent habitat, areas of high rodent density, and areas with open sewers.

The next phase of data collection, direct observation, would be conducted in a small sample (around 10) of households selected to represent a range of socioeconomic levels and household sizes, and a small sample of the most prevalent and high-risk occupations. A researcher would spend a day in each household and occupational setting and use a semistructured guide to make observations on the social and physical environment. Data collected through direct observation would then used to structure the content of in-depth interviews with a small sample of adults and key informants, who would be chosen based on age, education, occupation, and length of residence in the community. The focus of the interviews would be on eliciting explanatory models of leptospirosis, the ethnoecology (including theories of transmission) of the illness and its relationship to rats and water, rat control activities and general attitudes towards rats, and perceptions of current municipal rodent control measures and sanitation. A subsample of key informants selected based on their knowledge of and involvement in the community would also be chosen. These individuals would be questioned on multiple occasions throughout the study to expand on critical issues, define key concepts, and provide background to explain local perceptions and attitudes.

A small-scale structured survey of approximately 100 randomly sampled households would be conducted to collect data on demographic information, ethnomedical models of fevers, including leptospirosis, household and occupational patterns of water use, trash and wastewater disposal and storage, household and occupational activities involving contact with sewage, mud, rainwater, and floodwater, ethnoecology of leptospirosis, rats, and water, and attitudes and approaches towards both prevention of leptospirosis and rodent control.

Data-analysis procedures would include narrative analysis, content analysis, statistical inference, and cross-comparison of ethnographic and survey results. Content analysis of qualitative data would rely on identification of recurrent themes and patterns of belief and behavior. Survey data may be used to generate descriptive statistics and measures of association between selected variables. Ethnographic and survey variables could be compared to assess validity and juxtaposed to construct a robust picture of the community context of leptospirosis.

Such a study could be conceptualized as a qualitative / quantitative study that goes beyond the structured survey approach of case-control studies that have the goal of producing measures of association. The ecological framework explicitly addresses historical factors, narratives and behaviors of individuals, relevant physical and environmental characteristics of affected neighborhoods, and population-level demographic data, and looks at potential areas for intervention that would be acceptable to the affected communities.

Conclusion

While the focus of modern epidemiology on individual risk factors has resulted in important advances in our knowledge of health and disease transmission, the limitations inherent in this model have prompted many epidemiologists to consider developing new analytical frameworks for future research. Using both a meta-evaluation of the epidemiological literature critiquing the modern approach and a case study of one study recently conducted using a standard epidemiological design, I have identified two of the major limitations of risk factor epidemiology: a narrow, overly individualistic approach and a lack of consideration of a socio-historical context. In order to address these gaps in epidemiological research, it may be useful to adopt a multilevel perspective of the dynamics of health and disease in populations, an approach that has been termed "ecological" by many public health researchers[21, 23, 25, 26, 31, 44, 47]. In expanding the scope of epidemiological research in search of a more contextualized perspective, it may prove fruitful to cross disciplinary boundaries. Research in medical anthropology shares many of the goals of epidemiology and uses methods that could complement and enrich epidemiological data.

Susser's declaration that "the focus on risk factors at the individual level…will no longer serve"[23] is echoed here and supported with this critique and proposal for a more contextualized and interdisciplinary approach. Farmer points out that the history of infectious disease has "taught us that our approach must be dynamic, systemic, and critical"[48]. In calling for more contextual study of infectious disease, Farmer quotes a classic work by Eisenberg and Kleinman in which they propose: "the key task for medicine is not to diminish the role of the biomedical sciences in the theory and practice of medicine but to supplement them with an equal application of the social sciences in order to provide both a more comprehensive understanding of disease…The problem is not 'too much science' but too narrow a view of the sciences relevant to medicine"[49]. The study of leptospirosis epidemics in Salvador, Brazil is one specific example in which a broad perspective and integration of anthropological techniques will improve the quality and utility of epidemiologic research in improving the public's health.

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Afterword

The case-control study of leptospirosis has yielded important findings in addressing the public health problem of leptospirosis epidemics in Salvador, Brazil. Exposures were found to occur in both occupational and in residential settings, indicating a new epidemiologic pattern for a disease traditionally considered work-related. In cases that reported exclusively residential exposures, 40% were female, indicating that women may be just as susceptible to infection as men.

While advancing our knowledge of the transmission of leptospirosis during urban epidemics in Salvador, the findings of the case-control study are limited by the focus on individual behavior isolated from a socio-historical context. Using methods that account for the cultural, social and economic influences on individual behavior within may enrich the study of leptospirosis and guide successful intervention strategies in the future.