# Geographic Analysis of Pertussis Infection in an Urban Area: A Tool for Health Services Planning

*Carol Siegel, MD, MSPH, Arthur Davidson, MD, MSPH, Karen Kafadar, PhD, Jill M. Norris, PhD, MPH, James Todd, MD, and John Steiner, MD, MPH*

ABSTRACT

*Objective.* This study examined whether incident cases of pertussis cluster in urban census tracts and identified community characteristics that predict high-incidence areas.

*Methods.* An ecological study design was used. The study population included all persons diagnosed with pertussis from January 1, 1986, through December 31, 1994. Maps of rates were constructed via a geographic information system and clustering was statistically confirmed. Associations between pertussis rates and community characteristics were tested.

*Results.* Mapping and statistical analysis revealed spatial clustering of pertussis. Higher age-adjusted rates of pertussis infection were associated with higher proportions of residents below poverty level.

*Conclusions.* In urban areas, pertussis infection clusters in areas of poverty. (*Am J Public Health.* 1997;87:2022–2026)

## Introduction

Cyclic outbreaks of *Bordetella pertussis* have occurred during the past 15 years, despite an effective vaccine for infants and children,[1–3] and have resulted in significant morbidity and cost.[4–10] There are few data characterizing communities in which outbreaks occur.

This study used geographical techniques to determine whether incident cases of pertussis cluster within an urban area.[11–19] In addition, we examined whether poverty, race/ethnicity, the proportion of infants and children, population density, and population mobility are correlated with pertussis incidence.

## Methods

A retrospective surveillance system–based ecological design was used. Associations were examined between the outcome of interest (high rates of pertussis) and census tract characteristics.

The study was conducted in Denver, Colo, with a population of 467 610 and 180 census tracts in 1990. Demographic data were obtained from the 1990 US census.

Cases of Denver residents reported to the Colorado Department of Health with symptoms, laboratory findings, or both, meeting the Centers for Disease Control and Prevention (CDC) case definition of *B pertussis* infection from January 1, 1986, through December 31, 1994, were included as cases.[20] Additional cases were identified from the Colorado Hospital Association Discharge Database and confirmed by either chart review (21 cases, 10.7% of total) or *International Classification of Diseases,* 9th edition (ICD-9), coding alone (6 cases, 3% of total). For cases from the same address, the index case was the one with the earliest date of onset of symptoms.

We employed capture–recapture methods to estimate the efficiency of our case-ascertainment strategy.[21–23] The size of the "true" population of hospitalized pertussis patients and the proportion of this population captured by our data sources were estimated. Using previous estimates of pertussis hospitalization rates,[21] we estimated the coverage rate for all cases of pertussis.

The outcome variable was the age-adjusted incidence rate of pertussis infection for a census tract. By means of a geographic information system (MapInfo, Troy, NY), each case was assigned to a census tract according to the patient's address. This assignment was the basis for the census tract–specific age-adjusted rate, calculated by the direct method and based on the 1990 US population.[24] (Table 2 lists explanatory variables available for each census tract.)

Both exploratory mapping and confirmatory statistics were used to determine whether areas of increased pertussis incidence existed. In the exploratory mapping phase, the age-adjusted rates were smoothed by means of a nonlinear two-dimensional smoother.[25–27] The smoothed rates are subject to less variation, allowing detection of spatial patterns otherwise obscured by background "noise." Nonlinear smoothing is more likely than linear smoothing to reveal abrupt changes in rates. Maps were constructed from smoothed age-adjusted rates (MapInfo). To confirm that observed clusters were statistically significant, the Moran statistic for spatial autocorrelation was calculated.[28]

Descriptive statistics were calculated for age-adjusted rates and all explanatory variables. Bivariate associations between rates and explanatory variables were examined by calculating Pearson's or Spearman's

The authors are with the University of Colorado School of Medicine, Denver. Carol Siegel and Arthur Davidson are also with Community Health Services, Denver Department of Health and Hospitals.

Requests for reprints should be sent to Carol Siegel, MD, MSPH, University of Colorado Health Sciences Center, 4200 East 9th Ave, B-176, Denver, CO 80262.

This paper was accepted April 16, 1997.

correlation coefficient. A coefficient was considered significant at $P < .05$ (two-tailed test) (SAS software, SAS Institute, Inc, Cary, NC).

To elucidate the apparent spatial correlations, the rates were modeled as a linear function of census tract characteristics. A generalized linear regression model allowing for spatially correlated cases was fitted by means of Poisson regression (S-PLUS, Statistical Sciences, Seattle, Wash).[29] Transformations were applied to explanatory variables whose distributions were highly skewed. Residuals from this model revealed no spatial dependence, indicating the success of the model in accounting for the spatial correlation in the rates. Strata were determined by increasing levels of the apparently significant variable, and significant coefficients ($P < .05$) were confirmed by plotting rates pooled within a stratum against the median values of that variable for census tracts in the stratum.

## Results

From January 1, 1986, to December 31, 1994, 259 eligible cases of pertussis were reported to the Colorado Department of Health. Thirty-two additional patients with pertussis were admitted to three area hospitals, but these cases were not reported to the health department. Of these 291 patients, 261 (89.7%) resided in Denver, and 195 (74.7%) of the Denver cases were defined as index cases (Table 1).

The complete sample (261 patients) included 82.6% of infants and 83.0% of older persons in the theoretical "true" population of pertussis case patients. For index case patients alone, estimates of efficiency were 72.6% for children less than 1 year of age and 38.5% for those older than 1 year.

The age-adjusted annual rate was 4.66 cases of pertussis per 100 000 persons per year (95% confidence interval [CI] = 2.70, 6.62). The rate of hospitalized patients with pertussis was 1.93 per 100 000 persons per year (95% CI = 0.67, 3.19). Among census tracts, the rates were highly skewed. The median rate was 2.71 cases per 100 000 persons per year; the mean rate was 3.87, with a maximum rate of 18 and a minimum rate of 0 (43.4% of the census tracts).

Figure 1 maps the smoothed age-adjusted rates for 1986 through 1994. The highest density of cases occurred in the northern and western areas of the city. This pattern was also observed when only the cases in which patients were hospitalized were mapped (not shown). The Moran statistic for spatial autocorrelation was .134 (95% CI = .037, .232; $P = .002$).

Table 2 shows demographic characteristics of the census tracts and the associations between these characteristics and the rate of pertussis infection. Significant bivariate correlations ($P < .05$) are shown.

Before the Poisson regression was done, the independent variables were examined for correlations. A representative variable was chosen from highly correlated variables. The results of the Poisson regression are presented in Table 2; they indicate that when the other census tract characteristics are taken into account, increased rates of pertussis are associated with increased poverty and increased proportions of residents in the same house for 5 years (decreased mobility). A marginally significant association was also found with increased proportions of Hispanic residents within a census tract ($P = .06$). Subsequent analysis suggested a potentially spurious significance in the regression coefficient for the mobility index.

## Discussion

We found that incident cases of *B pertussis* infection showed geographic clustering in census tracts in an urban area. The age-adjusted incidence rates found in our study are comparable to those found previously.[1,4] In qualitative terms, the crescent area identified as having high rates of pertussis is also home to most of Denver's minority population and has the highest unemployment rate[30]; higher age-adjusted mortality rates from diabetes, human immunodeficiency virus (HIV) infection, homicide, and unintentional injury; and higher age-adjusted rates of fertility, late prenatal care, and low-birthweight births compared with other parts of Denver.[31] Thus, this area appears to be in need of preventive measures.

When various census tract characteris-

**TABLE 1—Demographic and Diagnostic Characteristics of Index Pertussis Cases, by Data Source: Denver, Colo, 1986 through 1994**

| | Population (%) in Denver[a] (n = 467 610) | Total Cases (n = 195) | Data Source: Colorado Department of Health (n = 168) | Data Source: Hospital Discharge Data[b] (n = 27) |
|---|---|---|---|---|
| | | No. (%) | No. (%) | No. (%) |
| Age | | | | |
| 0–12 mo | 6 106 (1.4) | 117 (60.0) | 93 (55.4) | 24 (88.9) |
| 13–35 mo | 15 081 (3.2) | 19 (9.2) | 17 (10.1) | 2 (7.4) |
| 3–11 y | 53 587 (11.4) | 15 (7.6) | 14 (8.3) | 1 (3.7) |
| >11 y | 392 836 (84.0) | 44 (22.5) | 44 (26.2) | 0 (63.0) |
| Patient's sex | | | | |
| Male | . . . | 89 (45.6) | 72 (42.9) | 17 (63.0) |
| Female | . . . | 106 (54.3) | 96 (57.1) | 10 (37.0) |
| Patient hospitalized | . . . | 82 (42.0) | 55 (32.7) | 27 (100.0) |
| Laboratory confirmation | . . . | 131 (67.1) | 119 (70.8) | 12 (44.4) |

[a]From the 1990 US census.
[b]Cases in which the patient was hospitalized but that were not reported to the Colorado Department of Health. The total number of cases in which the patient was hospitalized was 76.

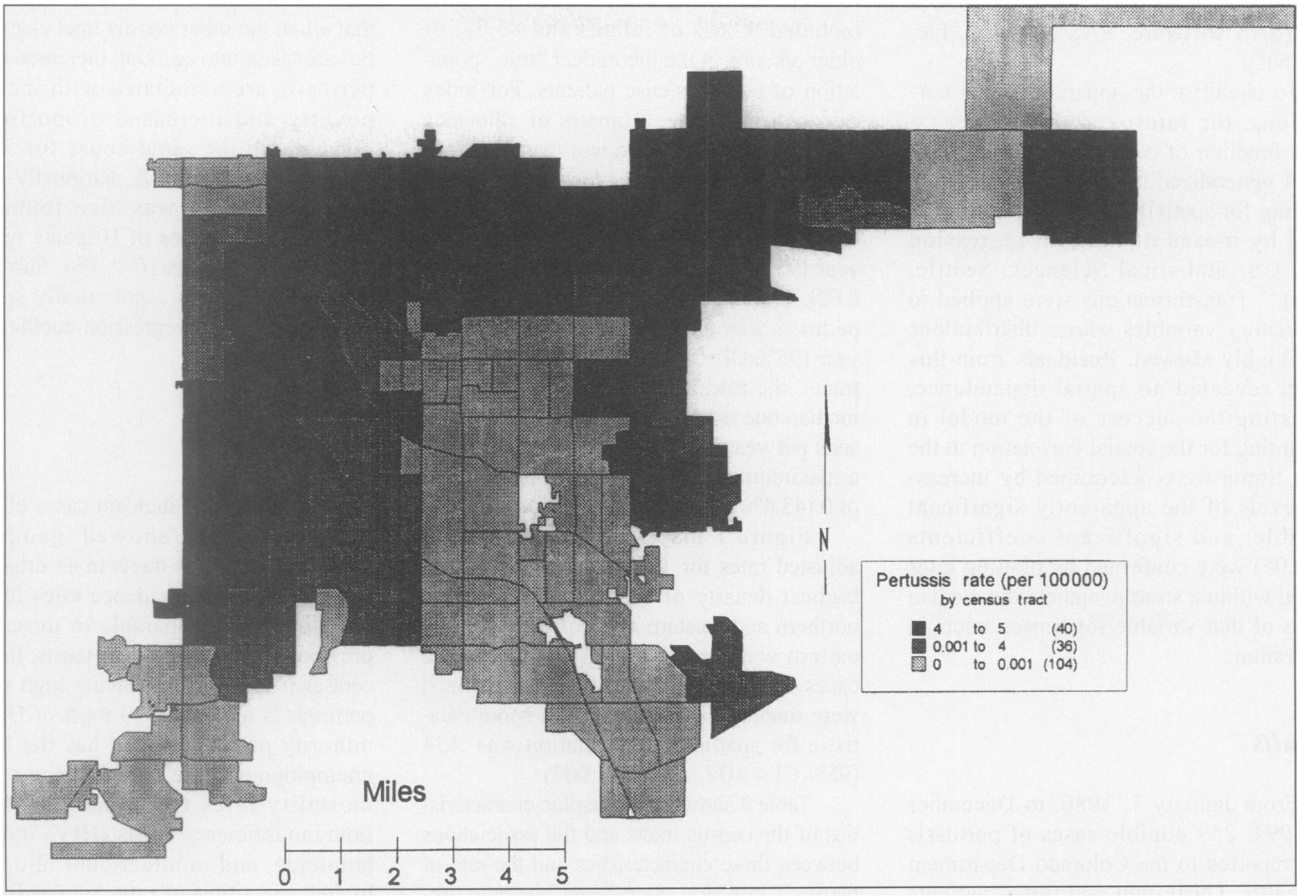


**FIGURE 1—Smoothed age-adjusted pertussis rates, Denver County, 1986 through 1994.**

tics were taken into account, we found an association between increased age-adjusted rates of pertussis infection and higher proportions of residents in the census tract living below the poverty level. A statistically weaker association was found between increased rates of pertussis and higher proportions of Hispanic residents. These findings may reflect poor access to preventive health care—in particular, pertussis immunization—or greater risk of exposure for these populations. Of the case

**TABLE 2—Characteristics of Census Tracts and Correlation between Mean Census Tract Characteristics and Age-Adjusted Rates of Pertussis Infection: Denver, Colo, 1986 through 1994**

| | Mean | SD | Correlation Coefficient[a] | P[b] | Adjusted Coefficient[c] | P[c] |
|---|---|---|---|---|---|---|
| Population per square mile | 603.1 | 350.6 | 0.21 | .02 | 0.07 | .47 |
| Median household income, $ | 26 660 | 11 684 | 0.38 | <.001 | ... | ... |
| Residents below poverty level, % | 17.24 | 14.46 | 0.45 | <.001 | 0 64 | <.001 |
| Residents receiving public assistance, % | 8.31 | 8.25 | 0.48 | .001 | ... | ... |
| Non-Hispanic White residents, % | 62.16 | 27.92 | −0.50 | <.001 | ... | ... |
| Hispanic residents, % | 21.75 | 21.72 | 0.40 | <.001 | 0.37 | .06 |
| Black residents, % | 12.83 | 21.21 | 0.11 | .18 | ... | ... |
| Female residents, % | 50.99 | 5.29 | 0.02 | .84 | 0.08 | .35 |
| Residents in same house for 5 y, % | 46.44 | 14.93 | 0.06 | .51 | 0.43 | .03 |
| Residents younger than 6 mo, % | 0.64 | 0.33 | ... | ... | 0.13 | .37 |

[a]Spearman or Pearson.
[b]For correlation coefficient.
[c]From the Poisson regression analysis.

patients with available immunization data, 50% of infants less than 6 months of age were unimmunized, and 78% of children aged 6 months through 5 years had not completed the primary immunization series (data not shown). Small area-specific immunization levels are not available. However, clinic assessment data from Denver Health, which provides primary care to most of Denver's poor, reveal full immunization for 30% of 2-year-olds in 1993 and 50% in 1994 (unpublished data, Denver Health). These data suggest that underimmunization is indeed responsible for some portion of the persistence of pertussis.

The analyses used in this study, including the mapping of smoothed rates, identify patterns that may not be apparent on simple inspection of maps of crude rates. No significant trends over time occurred during the study period (data not shown), and one outbreak affecting three households occurred. However, these analyses account for both of these possibilities.

The major limitation of this study is the underreporting of cases. We expanded our study population beyond those cases reported to the Colorado Department of Health by collecting discharge diagnosis information from the three hospitals with the majority of hospitalizations in the area, increasing our reporting efficiency to 83%. This generous estimate is probably due, in part, to lack of true independence of our two data sources; hospitalized case patients are probably more likely than outpatients to be reported to surveillance systems. Our improved efficiency may also be due to the liberal case definition used by the Colorado Department of Health,[32] as well as to vigilant disease-control units at area hospitals. It remains possible that our results were influenced by nonsystematic bias, in which better reporting occurs in more disadvantaged areas that are served by academic training hospitals. Using hospital discharge data, we constructed maps of cases in which the patients were hospitalized and found good concordance even in more affluent areas. These findings suggest a minimal impact of this bias.

The associations we found could be further evaluated by individual-level assessments of immunization status in communities. Mapping endeavors examining such issues of health care access as provider concentration would enhance such a study. As population-based sources of immunization information are developed, this strategy can yield valuable information for health care planners. □

## Acknowledgments

This study was supported in part by grant 5 D28 PE 50019 from the Division of Medicine of the Health Resources and Service Administration (HRSA; Dr Siegel) and by grant DMS95-10435 awarded to the University of Colorado, Denver, by the National Science Foundation (Dr Kafadar). Its contents are solely the responsibility of the authors and do not represent the views of HRSA or the National Science Foundation.

This study was presented in part at the annual meeting of the Pediatric Academic Societies, in Washington, DC, May 10, 1996.

The authors thank Mike Merino of Denver Public Health for his assistance with MapInfo; Peter Putnam, MD, and Noah Makovsky, MSII, for their assistance with chart review and data collection; Tim Englert of the Division of Disease Control at the Colorado Department of Health; Cliff Foster and Gary Knapp of the Biostatistics Division at Denver Public Health and the Colorado Hospital Association for providing data for analysis; and the Primary Care Research fellows at the University of Colorado for their thoughtful comments and support.

## References

1. Christie CD, Marx ML, Marchant CD, Reising SF. The 1993 epidemic of pertussis in Cincinnati: resurgence of disease in a highly immunized population of children. *N Engl J Med.* 1994;331:16–21.
2. Bass J, Wittler R. Return of epidemic pertussis in the United States. *Pediatr Infect Dis J.* 1994;13:343–345.
3. Centers for Disease Control and Prevention. Resurgence of Pertussis—United States, 1993. *MMWR Morb Mortal Wkly Rep.* 1995;42:952–953.
4. Centers for Disease Control and Prevention. Pertussis—United States, January 1992–July 1995. *MMWR Morb Mortal Wkly Rep.* 1995;44:525–529.
5. Cromer BA, Goydos J, Hackell J, Mezzatesta J, Dekker C, Mortimer EA. Unrecognized pertussis infection in adolescents. *Am J Dis Child.* 1993;147:575–577.
6. Mink CA, Sirota NM, Nugent S. Outbreak of pertussis in a fully immunized adolescent and adult population. *Arch Pediatr Adolesc Med.* 1994;148:153–157.
7. He Q, Viljanen MK, Nikkari S, Lyytikainen R, Mertsola J. Outcomes of *Bordetella pertussis* infection in different age groups of an immunized population. *J Infect Dis.* 1994;170: 873–877.
8. Centers for Disease Control and Prevention. Transmission of pertussis from adult to infant—Michigan, 1993. *JAMA.* 1995;273:768.
9. Wortis N, Strebel PM, Wharton M, Bardenheier B, Hardy IRB. Pertussis deaths: report of 23 cases in the United States, 1992 and 1993. *Pediatrics.* 1992;97:607–612.
10. Pichichero ME, Treanor J. Economic impact of pertussis. *Arch Pediatr Adolesc Med.* 1997;151:35–40.
11. Alexander FE, Cuzick J. Methods for the assessment of disease clusters. In: Elliott P, Cuzick J, English D, Stern R, eds. *Geographical and Environmental Epidemiology: Methods for Small Area Studies.* New York, NY: Oxford University Press; 1992:238–250.
12. Rothenberg RB, Steinberg KK, Thacker SB. The public health importance of clusters: a note from the Centers for Disease Control. *Am J Epidemiol.* 1990:132(Suppl 1);S3–S5.
13. Kerner JF, Andrews H, Zauber A, Struening E. Geographically based cancer controls: methods for targeting and evaluating the impact of screening interventions on defined populations. *J Clin Epidemiol.* 1988;41:543–553.
14. Ross A, Davis S. Point pattern analysis of the spatial proximity of residences prior to the diagnosis of persons with Hodgkins disease. *Am J Epidemiol.* 1990;132(Suppl 1):S53–S62.
15. Siemiatycki J, Colle E, Aubert D, Campbell S, Delmonte MM. The distribution of type 1 (insulin-dependent) diabetes mellitus by age, sex, secular trend, seasonality, time clusters, and space clusters: evidence from Montreal, 1971–1983. *Am J Epidemiol.* 1986;124: 545–560.
16. Skrimshire AM. A small area analysis of self-poisoning and self-injury in the region of Oxford. *J Biosoc Sci.* 1976;8:85–112.
17. Weiss KB, Wagener DK. Geographic variations in US asthma mortality: small area analysis of excess mortality, 1981–85. *Am J Epidemiol.* 1990;132(Suppl 1):S107–S115.
18. Florin J. Introduction. In: Rickets TC, Savitz LA, Gesler WM, Osborne DM, eds. *Geographic Methods for Health Services Research.* Lanham, Md: University Press of America; 1994:1–10.
19. Wennberg J, Gittelsohn A. Small area variation in health care delivery. *Science.* 1973; 182:1102–1108.
20. Wharton M. Case definitions for public health surveillance. *MMWR Morb Mortal Wkly Rep.* 1990; 39(Rr-13):1–43.
21. Sutter RF, Cochi SL. Pertussis hospitalizations and mortality in the United States, 1985–1988: Evaluation of the completeness of national reporting. *JAMA.* 1992;267:386–391.
22. Wittes JT, Colton T, Sidel VW. Capture-recapture methods for assessing the completeness of case ascertainment when using multiple information sources. *J Chronic Dis.* 1974;27:25–36.
23. Chapman DG. Some properties of the hypergeometric distribution with applications to zoological sample censuses. Berkeley, Calif: University of California Publications in Statistics; 1951;1:131–160.
24. Rothman KJ. Standardization of rates. In: Rothman K. ed. *Modern Epidemiology.* Boston, Mass: Little, Brown & Co; 1986:41–49.
25. Goodall CR. A survey of smoothing techniques. In: Fox J, Long JS, eds. *Modern Methods of Data Analysis.* Beverly Hills, Calif: Sage Publications; 1990:126–176.
26. Hansen KM. Headbanging: robust smoothing in the plane. *IEEE Trans Geoscience Remote Sensing.* 1991;29:369–378.
27. Goodall CR, Hansen KM. Resistant smoothing in higher dimensions. In: *Proceedings of the American Statistical Association Section on Statistical Graphics.* Washington, DC: American Statistical Association; 1988:17–21.

28. McShane LM, Albert PS, Palmatier MA. A latent process regression model for spatially correlated count data. *Biometrics.* 1997;53: 301–309.
29. Cliff AD, Ord JK. Some measures of autocorrelation in the plane. In: Cliff AD, Ord JK. *Spatial Autocorrelation.* London, England: Pion Ltd; 1981.
30. *Denver Atlas II.* Denver, Colo: Information Services Division, City and County of Denver; 1994.
31. Davidson AJ, Doescher MP, Knapp G, Foster CT, Wright RA. County-wide small area analyses: estimation of denominators for users of a county health care agency and their application in health status measures. In: *Proceedings of the 1993 Public Health Conference on Records and Statistics.* Washington, DC: Public Health Service; 1994. DHHS Pub PHS 94-1214:244–248.
32. Sacks JJ. Utilization of case definitions and laboratory reporting in the surveillance of notifiable communicable diseases in the United States. *Am J Public Health.* 1985;75: 1420–1422.


# The Epidemiology of Necrotizing Enterocolitis Infant Mortality in the United States

*Robert C. Holman, MS, Barbara J. Stoll, MD, Matthew J. Clarke, MA, and Roger I. Glass, MD, PhD*


## ABSTRACT

*Objectives.* This study examined trends and risk factors for infant mortality associated with necrotizing enterocolitis in the United States.

*Methods.* Necrotizing enterocolitis-associated deaths and infant mortality rates from 1979 through 1992 were determined by means of US multiple cause-of-death and linked birth/infant death data.

*Results.* Annual necrotizing enterocolitis infant mortality rates decreased from 1979 through 1986 but increased thereafter and were lower during the 3-year period before (1983 through 1985; 11.5 per 100 000 live births) the introduction of surfactants than after (1990 through 1992; 12.3 per 100 000). Low-birthweight singleton infants who were Black, male, or born to mothers younger than 17 had increased risk for necrotizing enterocolitis-associated death.

*Conclusions.* As mortality among low-birthweight infants continues to decline and smaller newborns survive early causes of death, necrotizing enterocolitis-associated infant mortality may increase. (*Am J Public Health.* 1997;87:2026-2031)


## *Introduction*

Necrotizing enterocolitis is the most common condition for which emergency gastrointestinal surgery is required during the neonatal period and an important cause of both morbidity and mortality in the preterm infant.[1–4] Despite extensive epidemiological, clinical, and basic research, the cause of necrotizing enterocolitis remains unproven. It is generally accepted that prematurity places the newborn at substantially increased risk for the condition,[3] and increased case rates are associated with decreasing birthweight and gestational age.[4] Moreover, necrotizing enterocolitis is unusual in the first few days of life and is primarily a disease of preterm infants who have survived the immediate neonatal period. Recent advances in neonatal intensive care have led to increased survival of smaller, more immature infants, who are at greatest risk for necrotizing enterocolitis.

In 1989, analysis of US death certificate data showed that annual infant mortality rates for necrotizing enterocolitis decreased from 14.5 deaths per 100 000 live births in 1979 to 10.2 deaths per 100 000 live births in 1985.[5] Since 1985, both neonatal and infant mortality rates have declined.[6] The introduction of exogenous surfactant in the early 1990s has been associated with a decrease in mortality among low-birthweight (<2500 g) infants.[7] The present study was undertaken to describe current trends in infant mortality associated with necrotizing enterocolitis, to evaluate selected infant and parental characteristics that may be associated with necrotizing enterocolitis death, and to compare necrotizing enterocolitis infant mortality rates in the pre- and post-surfactant eras.

## *Methods*

Multiple cause-of-death and natality data for 1979 through 1992 and linked data for births and infant deaths for 1983 through 1991 were obtained from the National Center for Health Statistics, Centers for Disease Control and Prevention.[8–22] On the basis of the ninth revision of the *International Classification of Diseases* (ICD),[23] necrotizing enterocolitis infant (<1 year of age) deaths were defined as deaths for which ICD-9 code 777.5 was recorded anywhere on the death certificate.

The multiple cause-of-death and natality[10] data were used to determine the number of necrotizing enterocolitis deaths and annual infant mortality rates. Necrotizing enterocolitis infant mortality rates, calculated as the number of deaths per 100 000 live births, were determined overall and by race, sex, and standard region. The neonatal period was defined as less

Robert C. Holman, Matthew J. Clarke, and Roger I. Glass are with the Division of Viral and Rickettsial Diseases, National Center for Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, Ga. Barbara J. Stoll is with the Division of Neonatal-Perinatal Medicine, Department of Pediatrics, Emory University School of Medicine, Atlanta, Ga.

Requests for reprints should be sent to Robert C. Holman, MS, Division of Viral and Rickettsial Diseases, National Center for Infectious Diseases, Centers for Disease Control and Prevention, MS A39, Atlanta, GA 30333.

This paper was accepted November 1, 1996.