Infectious Disease Mortality among Infants in the United States, 1983 through 1987

ABSTRACT

Objectives. The purpose of this study was to determine the relative importance of infectious disease as a cause of infant mortality in the United States and to identify characteristics at birth associated with subsequent infectious disease mortality.

Methods. Birth and infant death certificate data from the National Center for Health Statistics (NCHS) 1983 through 1987 Linked Birth/Infant Death Data Sets were analyzed.

Results. Infection was the underlying cause of death for over 16 000 infants, representing the fourth leading cause of mortality in this cohort. Almost 90% of infectious disease deaths during infancy were due to noncongenital infections, and the majority of these deaths occurred during the postneonatal period. Low birthweight, preterm birth, and male gender were independently associated with postneonatal mortality due to noncongenital infection.

Conclusions. NCHS should revise its classification system for causes of infant mortality to incorporate an "Infectious Diseases" category. Future research should be directed toward clarifying the low birthweight–infectious disease mortality relationship and determining the degree to which infection-related infant deaths might be prevented by existing vaccines or improved access to health care. (*Am J Public Health.* 1997;87:192–198)

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Introduction

While infection is responsible for a large proportion of infant deaths in developing countries,[1] it is not perceived as a significant cause of infant mortality in the United States. Indeed, while congenital anomalies and sudden infant death syndrome have been consistently ranked as the two most common causes of infant mortality in this country, infectious diseases have been ranked much lower.[2–6] For example, septicemia and meningitis have been ranked between the 12th and the 15th leading causes of infant mortality.[2–6] However, while the prevention of deaths due to congenital anomalies and sudden infant death syndrome remains an important but as yet unrealized goal, the prevention of deaths due to infectious disease may already be feasible. The goals of this study were to determine the relative importance of infectious diseases as a cause of infant mortality in the United States and to identify characteristics at birth that are associated with infectious disease mortality during infancy.

Materials and Methods

Linked Birth/Infant Death Data Sets: 1983 through 1987 Birth Cohorts

Beginning with the 1983 US birth cohort, the National Center for Health Statistics linked individual birth and infant death certificates to create the Linked Birth/Infant Death Data Sets. The methodology for the creation of these data sets is described in detail in the documentation for the Linked Birth/Infant Death Data Sets.[7–11] Briefly, each data set includes two data files: a numerator file including linked records of live births and infant deaths for the birth cohort of the specified calendar year and a denominator file including records of live births for this cohort. Each data set contains information about individuals born in a given year who died before their first birthday. If no death certificate was filed, the infant was assumed to have survived. Each data set includes records for births and infant deaths that occurred in the United States to both US residents and nonresidents. In 1983 and 1984, only 50% of the birth certificates in five areas (Arizona, California, Delaware, Georgia, and the District of Columbia) were coded for the denominator file. A system of record weighting for the birth records from these five areas was used; this system is described in detail in the documentation for the 1983 and 1984 data sets.[7–8]

The 1983 through 1987 Linked Birth/Infant Death Data Sets contain data from 18 656 519 birth certificates and 192 503 infant death certificates. Approximately 98% of infant death certificates were linked to birth certificates in the 1986 and 1987 birth cohorts. Similar data are not available for the 1983 through 1985 cohorts. The study population was limited to those infants classified as US residents.

Classification of Cause of Death and Definitions

All underlying cause of death data in the 1983 through 1987 linked files were

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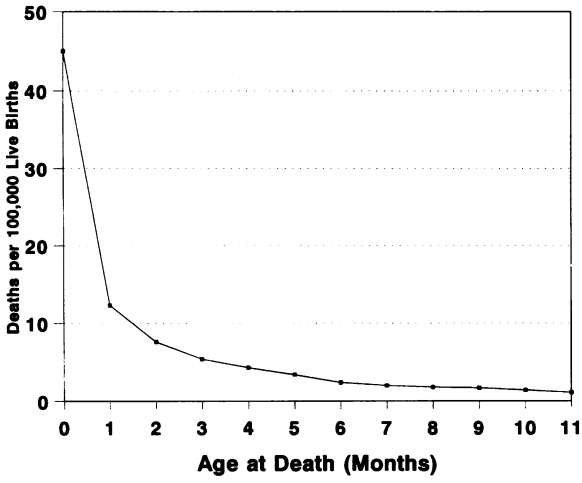
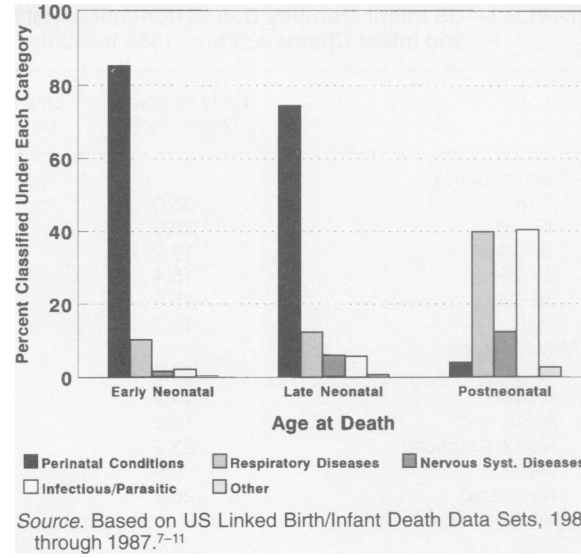


Source. Based on US Linked Birth/Infant Death Data Sets, 1983 through 1987.[7–11]

FIGURE 1—US infectious disease death rate among infants, by age at death, 1983 through 1987.



Source. Based on US Linked Birth/Infant Death Data Sets, 1983 through 1987.[7–11]

FIGURE 2—Percentage distribution of specific types of US noncongenital infectious disease deaths among infants, by age at death, 1983 through 1987.

coded according to the *International Classification of Diseases,* ninth revision (ICD-9).[12] Subsequently, additional ICD-9 codes (042.0–044.9) were introduced to classify human immunodeficiency virus (HIV) infection as a cause of death.[13] ICD-9 codes were defined a priori as representing a noninfectious or infectious disease. Infectious diseases were further classified as representing a congenital infection or, in the absence of information indicating congenital infection, a noncongenital infection. (A list of the ICD-9 codes defined as representing congenital infection and noncongenital infection are available from the authors.) Some of these codes ultimately had no deaths associated with them. All other ICD-9 codes were designated as representing noninfectious conditions.

The residence of the infant was defined as the usual place of residence of the mother. Early neonatal deaths were defined as those occurring at an age of less than 7 days. Late neonatal deaths were defined as those occurring between the ages of 7 and 27 days. Postneonatal deaths were defined as those occurring at 28 days or more. Preterm birth was defined as birth before 37 completed weeks of gestation. Very low birthweight was defined as a birthweight of less than 1500 g. Moderately low birthweight was defined as a birthweight of 1500 g or more but less than 2500 g. Geographic regions of the United States were defined according to the four standard census regions: Northeast, Midwest, West, and South.[7–11]

Analysis

Although analysis of mortality data is usually performed with survival analysis, categorical analyses of the data are presented in this paper for ease of presentation and comprehension. Univariate relationships were statistically evaluated with the chi-square test.[14,15] Ordered trends of proportions were appraised with the chi-square test for trend.[14,15] Odds ratios were calculated to estimate the strength of the associations between maternal and infant characteristics and postneonatal mortality due to noncongenital infection. Because of the low risk of death in the cohort, the odds ratios approximated relative risks.[14,15] Ninety-five percent confidence intervals for odds ratios were calculated by Woolf's method.[14,15] Adjusted odds ratios were calculated by logistic regression. Regression coefficients and their standard errors were used to estimate the magnitude and 95% confidence interval for each adjusted odds ratio.[14,15] All statistical tests were interpreted in a two-tailed fashion to estimate *P* values and 95% confidence intervals. Data analysis was performed with the Statistical Analysis System.[16]

Results

Incidence of Infectious Disease Deaths

From 1983 through 1987, 18 635 733 US resident births occurred and 192 388 infant deaths occurred, resulting in an all-cause infant death rate of 1032 deaths per 100 000 live births. Of these deaths, 16 511 (9%) were due to infectious diseases, generating an infant death rate due to infectious diseases of 89 deaths per 100 000 live births. The annual death rate due to infectious diseases decreased from 93 deaths per 100 000 live births in 1983 to 86 deaths per 100 000 live births in 1987 ($P < .001$). Of the infant deaths due to infectious diseases, 1694 (10%) were classified as due to congenital infections and 14 817 (90%) as due to noncongenital infections. An increase in the annual death rate due to congenital infection from 8.3 deaths per 100 000 live births in 1983 to 9.5 deaths per 100 000 live births in 1987 ($P = .17$) was accompanied by a decrease in the annual death rate due to noncongenital infection from 85 deaths per 100 000 live births in 1983 to 77 deaths per 100 000 live births in 1987 ($P < .001$).

Age Distribution of Infectious Disease Deaths

As illustrated in Figure 1, the aggregate infectious disease mortality rate

TABLE 1—US Infant Mortality Due to Noncongenital Infection, by Maternal and Infant Characteristics, 1983 through 1987

	Early Neonatal Death Rate[a]	Late Neonatal Death Rate[b]	Postneonatal Death Rate[c]
Maternal age, y			
≤16	35.0	41.3	97.6
17–19	28.0	27.0	70.4
20–24	19.9	20.0	49.8
25–29	15.4	13.9	34.0
30–34	15.9	13.4	29.6
≥35	16.7	17.1	34.6
Maternal race			
Black	33.8	41.7	96.4
White	15.9	13.4	32.7
Asian	13.8	14.4	37.2
Native American	23.2	19.2	98.5
Other	9.9	40.0	30.0
Not stated	26.1	17.7	45.7
Maternal education, y			
<9	26.6	28.2	84.3
9–11	27.2	27.7	81.6
12	18.5	17.3	40.2
13–15	16.3	14.2	28.9
≥16	12.4	10.2	19.1
Unknown	18.4	18.6	44.0
Mother's marital status			
Unmarried[d]	29.6	31.0	76.7
Married	15.6	13.5	32.3
No. prenatal visits			
<5	67.5	70.0	152.1
5–9	29.0	27.2	59.6
≥10	9.7	8.2	26.2
Unknown	20.9	23.3	46.3
Trimester prenatal care began			
First	16.7	15.0	34.0
Second	19 1	21.1	60.4
Third	15.0	16.3	73.6
Unknown or no care	59.4	60.0	114.9
Infant's gender			
Male	20.9	20.3	49.1
Female	16.5	15.3	37.2
Gestational age			
Preterm	125.6	120.4	171.7
Term	6.0	6.0	28.3
Unknown	41.5	42.7	77.7
Birthweight			
Very low[e]	606.4	1088.9	1239.9
Moderately low[f]	97.1	58.4	127.9
Normal	6.1	5.6	27.6
Unknown	199.6	83.1	237.8
Plurality			
Singleton	17.7	16.3	41.3
Twin	65.7	90.9	139.0
Other multiple	87.9	233.4	224.5
Live birth order			
Fourth or later	21.5	21.7	68.6
Third	17.5	17.0	51.5
Second	16.2	16.4	41.8
First	20.3	18.3	35.5
Not stated	45.9	34.0	49.0
Geographic region of residence at birth			
Northeast	17.6	15.6	37.9
Midwest	17.4	15.4	37.1
South	22.7	21.4	52.6
West	15.0	16.9	40.1

[a]Number of deaths per 100 000 live births.
[b]Number of deaths per 100 000 early neonatal survivors.
[c]Number of deaths per 100 000 late neonatal survivors.
[d]Single, divorced, or separated.
[e]Less than 1500 g.
[f]Between 1500 and 2500 g.

varied during infancy. The rate of infant death due to infectious diseases decreased from 45 deaths per 100 000 live births during the 1st month of life to 1.1 deaths per 100 000 live births during the 12th month of life.

In addition, the proportion of all infant deaths due to infection varied according to age at death. Infectious diseases were responsible for 4.7% of early neonatal deaths, 17.0% of late neonatal deaths, and 12.0% of postneonatal deaths. The largest number of infectious disease deaths occurred in the postneonatal period (n = 8119).

The distribution of age at death for infectious disease deaths differed substantially from the distribution for all infant deaths. While the majority (54%) of all infant deaths occurred during the early neonatal period, almost half (49%) of all infectious disease deaths occurred during the postneonatal period. Over half (54%) of noncongenital infection deaths occurred during the postneonatal period, but 82% of deaths due to congenital infection occurred during the early neonatal period.

Categorization and Characteristics of Infectious Disease Deaths

More than 97% of infant deaths due to congenital infections were ascribed to causes of death whose ICD-9 codes are categorized under "perinatal conditions." Of the infectious disease deaths not due to congenital infection, the categorization of underlying cause of death ICD-9 codes varied according to when during infancy death occurred. As illustrated in Figure 2, early neonatal deaths were predominantly categorized under "perinatal conditions," while the majority of postneonatal deaths were categorized under "infectious or parasitic diseases" or under specific organ systems, for example, "respiratory diseases."

Infectious disease deaths were further analyzed according to causative organism and location of the infection. Unfortunately, location of the infection was unspecified for many congenital infection deaths (91%) and noncongenital infection deaths in the early (81%) and late (46%) neonatal periods. In contrast, location of the infection was specified in over 91% of postneonatal noncongenital infection deaths. Of these infections, 38% were localized to the lower respiratory tract, 22% were generalized (e.g., sepsis), 14% were localized to the central nervous system, and almost 10% were localized to the gastrointestinal tract.

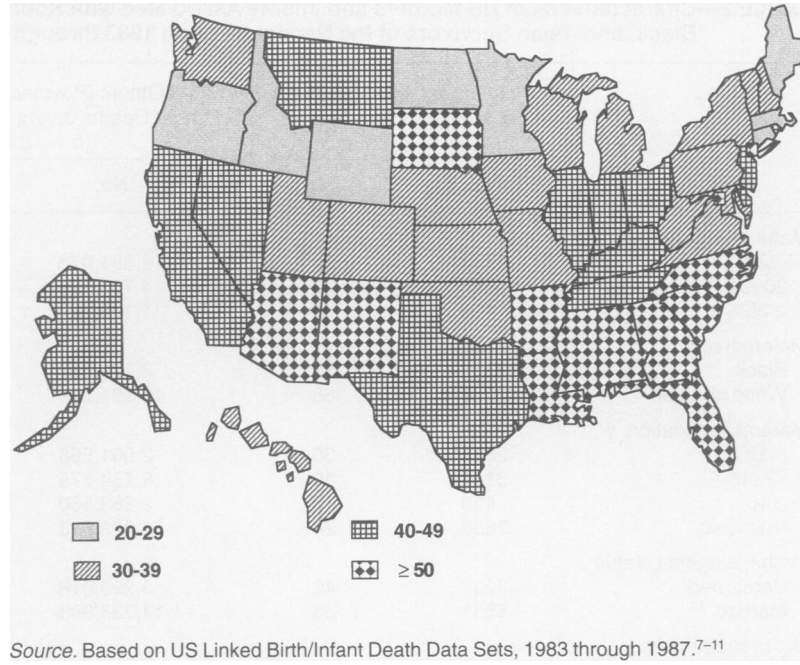
Most infectious disease deaths occurred among hospitalized patients. However, the proportion of infectious disease deaths among outpatients increased during infancy, from less than 1% of early neonatal infectious disease deaths to 12% of postneonatal infectious disease deaths.

An autopsy was performed in a minority of infant deaths due to congenital infections (38%) and early and late neonatal deaths due to noncongenital infections (45% and 44%, respectively). In contrast, over 60% of postneonatal noncongenital infection deaths underwent autopsy.

Noncongenital Infection Death Rates

As illustrated in Table 1, noncongenital infection death rates were associated with several maternal and infant characteristics. Increased infectious disease death rates occurred among infants of young mothers, especially those aged 16 years or younger. The highest rates of infectious disease deaths during the early and late neonatal periods occurred among infants of Black mothers, and the highest rates of infectious disease death during the postneonatal period occurred among infants of Black or Native American mothers. Infants of mothers with less than a high school education, especially those with less than a ninth-grade education, experienced higher death rates than infants of mothers with more education. Similarly, infants of unmarried mothers had higher infectious disease death rates than did infants of married mothers. The highest rates of infectious disease deaths for infants of all ages occurred among mothers with few prenatal visits. Finally, infants of mothers with no prenatal care or whose prenatal care status was unknown experienced the highest infectious disease death rates during all three periods, and infants whose mothers began receiving prenatal care late in pregnancy experienced elevated infectious disease death rates during the postneonatal period.

Infectious disease death rates were consistently higher for male than for female infants and for preterm than for term infants. Moderately low-birthweight infants and, in particular, very low-birthweight infants had higher infectious disease death rates than did normal-birthweight infants. Multiple-gestation births also had higher infectious disease death rates than did singleton births. A trend of increasing infectious disease death rates with increasing live birth order was observed among infants who died in the postneonatal period. Finally, infants born in the South experienced increased infectious disease death rates throughout infancy.



Source. Based on US Linked Birth/Infant Death Data Sets, 1983 through 1987.[7–11]

FIGURE 3—US postneonatal mortality (deaths per 100 000 infants alive at beginning of postnatal period) due to noncongenital infections, by state, 1983 through 1987.

Death rates in relation to geographic location of residence at the time of birth were examined in greater detail for noncongenital infection deaths during the postneonatal period. As illustrated in Figure 3, the highest postneonatal noncongenital infection mortality rates occurred among infants born in the District of Columbia, New York City, eight southern states (Arkansas, Louisiana, Mississippi, Alabama, Georgia, Florida, South Carolina, North Carolina), and three other states (New Mexico, Arizona, and South Dakota).

Determinants of Postneonatal Noncongenital Infection Deaths

Univariate and multivariate analyses of potential determinants of postneonatal noncongenital infectious disease deaths among Whites, Blacks, and Asians are summarized in Table 2. These analyses suggest that several factors were associated with an increased risk of postneonatal mortality due to noncongenital infection. Specifically, younger mothers, Black mothers, less educated mothers, unmarried mothers, and mothers with few prenatal visits or prenatal care that began late in pregnancy had infants at increased risk of death due to infection in the postneonatal period. Also, male gender, preterm birth, low birthweight, and increasing live birth order were associated with an elevated risk of death from noncongenital infection in the postneonatal period.

Discussion

Over 16 000 infants in this recent 5-year US birth cohort died as a result of infection. The relative importance of infection as a cause of infant mortality is more clearly appreciated when infectious diseases are considered in the aggregate, as in this analysis, than when specific categories of infectious diseases are ranked separately as causes of infant mortality (e.g., "infections specific to the perinatal period" [ICD-9 code 771], "pneumonia and influenza" [ICD-9 codes 480–487], "septicemia" [ICD-9 code 038], and "meningitis" [ICD-9 codes 320–322]).[2–6] Infection, considered in the aggregate, caused 9% of infant deaths in this cohort and represented the fourth leading cause of death, after congenital anomalies (n = 40 981), sudden infant death syndrome (n = 25 911), and respiratory distress syndrome (n = 17 250). Infection

TABLE 2—Characteristics of US Mothers and Infants Associated with Noncongenital Infection Deaths among White, Black, and Asian Survivors of the Neonatal Period 1983 through 1987

	Postneonatal Deaths due to Infectious Diseases (n = 7788)		All Others (Postneonatal Survivors and Other Deaths during Postneonatal Period) (n = 18 232 521)		
	No.	%	No.	%	Adjusted OR (95% CI)[a]
Maternal age, y					
<20	1738	22	2,331,075	13	1.60 (1.42, 1.80)
20–34	5646	73	14,708,226	81	1.22 (1.10, 1.35)
≥35	404	5	1,193,220	7*	Reference
Maternal race					
Black	2732	35	2,870,807	16	1.45 (1.37, 1.53)
White or Asian	5056	65	15,361,714	84*	Reference
Maternal education, y					
<12	2315	30	2,861,568	16	1.84 (1.65, 2.05)
12–15	3140	40	8,734,775	48	1.33 (1.20,1.47)
≥16	453	6	2,363,560	13*	Reference
Unknown	1880	24	4,272,618	23	1.56 (1.40, 1.75)
Mother's marital status					
Unmarried	3237	42	3,993,618	22	1.22 (1.15, 1.29)
Married	4551	58	14,238,903	78*	Reference
No. prenatal visits					
<5	1588	20	1,053,163	6	1.59 (1.48, 1.72)
5–9	2149	28	3,643,713	20	1.28 (1.20, 1.36)
≥10	2811	36	10,853,536	60*	Reference
Unknown	1240	16	2,682,109	15	1.16 (1.06, 1.27)
Trimester prenatal care began					
Third	508	7	709,379	4	1.24 (1.12, 1.36)
Second	1913	25	3,199,205	18	1.13 (1.07, 1.20)
First or no care	5064	65	13,948,717	77*	Reference
Unknown	303	4	375,220	2	1.17 (1.02, 1.34)
Infant's gender					
Male	4535	58	9,336,916	51	1.38 (1.32, 1.45)
Female	3253	42	8,895,605	49*	Reference
Gestational age, wk					
<25	393	5	30,430	0	3.20 (2.82, 3.63)
25–36	2417	31	1,611,294	9	1.42 (1.33, 1.52)
≥37	4423	57	15,866,205	87*	Reference
Unknown	555	7	724,592	4	1.38 (1.25, 1.53)
Birthweight					
Very low[b]	1840	24	146,760	1	22.83 (21.12, 24.68)
Moderately low[c]	1287	16	1,008,164	6	3.23 (3.01, 3.46)
Normal	4617	59	17,062,627	94*	Reference
Unknown	44	1	14,970	0	8.22 (6.10, 11.09)
Live birth order					
Third or greater	2596	33	4,561,627	25	1.65 (1.55, 1.75)
Second	2486	32	6,007,335	33	1.38 (1.30, 1.46)
First or not stated	2706	35	7,663,559	42*	Reference

Note. OR = odds ratio; CI = confidence interval.
[a]All variables listed in this table were included in the logistic regression model.
[b]Less than 1500 g.
[c]Between 1500 and 2500 g.
*$P < .01$.

also accounted for 12% of postneonatal deaths and was the third leading cause of death in this cohort, after sudden infant death syndrome (n = 24 160) and congenital anomalies (n = 10 599).

In light of the relative importance of infectious diseases (considered in the aggregate) as a cause of infant mortality in this country, the National Center for Health Statistics should revise its classification system for causes of infant mortality to incorporate a new category: "infectious diseases." There would be some heterogeneity inherent in such a category, but, arguably, no more than with the current classification system, in which the category "congenital anomalies," the leading cause of death in infancy, includes many different anomalies. Creation of a new category to include all infectious causes of death would help clarify the importance of infectious diseases as a cause of infant mortality in this country and, in doing so, would serve to focus

research and public health interventions on prevention of these deaths.

The introduction of *Haemophilus influenzae* type b vaccines, especially conjugate vaccines for administration in infancy, has resulted in a dramatic decline in the occurrence of serious, invasive infections (e.g., meningitis[17]) due to this common pediatric pathogen. Therefore, our results should be replicated among more recent birth cohorts to determine whether the relative importance of infections as a cause of infant mortality has changed since 1987.

Almost 90% of the infectious disease deaths during infancy in this cohort were due to noncongenital infections. Several sociodemographic characteristics of infants in this cohort with higher death rates due to noncongenital infection have been found to be associated with infant mortality in general (e.g., maternal race and education[18]) or with infant mortality due to specific infections. Studies in the United States have identified positive associations between infant mortality due to diarrhea and non-White race,[19,20] residence in the South,[20] late or inadequate prenatal care,[19,20] unmarried status of the mother,[19,20] low maternal educational attainment,[20] young maternal age,[20] and birth of another child within the previous 3 years.[20] In Brazil, infant death due to respiratory infection has been associated with low socioeconomic status, young maternal age, and the number of children under the age of 5 years in the household.[21] Our results also revealed elevated noncongenital infection death rates among infants of low birthweight or male gender and among preterm infants, suggesting a possible relationship between biologic factors and infectious disease mortality during infancy. Alternatively, at least part of the increased risk associated with low birthweight may represent the effects of socioeconomic status, which could not be completely controlled for in the analysis.

As the majority of noncongenital infection deaths occurred during the postneonatal period, the relationship between both sociodemographic and biologic factors and infectious disease mortality was explored further among postneonatal deaths. Our findings confirm those of previous studies that have emphasized the association between sociodemographic variables and either overall[22–25] or infectious disease–related[26,27] postneonatal mortality. However, again, our results suggest that biologic factors such as low birthweight, preterm birth, and male gender are independently associated with an increased risk of postneonatal mortality due to noncongenital infection. Although a relationship between low birthweight and infectious disease mortality has been described,[19,28–30] to our knowledge, associations between infectious disease mortality and either preterm birth or male gender have not previously been recognized.

The Linked Birth/Infant Death Data Sets represent a valuable resource for infant mortality research and provide the most comprehensive data available for this exploratory analysis of infant mortality due to infection in the United States. It is important, however, to acknowledge the potential limitations of vital records data, both in general and with regard to the specific data used for this analysis. First, it is well recognized that the accuracy and completeness of birth and death certificate data are often suboptimal.[31] The Linked Birth/Infant Death data lack specificity with regard to the causative organism, location of the infection, and, if the infant was an inpatient at the time of death, length of hospitalization and amount of surgery or instrumentation prior to death. The lack of detailed information concerning the events surrounding death makes it difficult to ascertain the likelihood of misclassification of the cause of death listed on the death certificate. One example, albeit much more likely to have occurred in previous decades than in the 1980s, is misclassification of deaths due to sudden infant death syndrome as deaths due to pneumonia. Also, since these data sets contain only limited information regarding socioeconomic status, only proxy variables such as maternal education can be evaluated.

Thus, research should be pursued to obtain a better understanding of the risk factors for infectious disease mortality during infancy and to identify potential preventive strategies. As would be expected, the great majority of deaths due to congenital infection occurred during the early neonatal period. In many of these cases, as well as many of the early neonatal deaths due to noncongenital infections, death occurred within the first few hours of life. Prevention of these deaths would, in many cases, require the identification of at-risk mothers well before the time of delivery. It is unlikely that information acquired at birth could or should be used to target these newborns for interventions intended to decrease the likelihood of infectious disease mortality. For example, factors such as preterm birth and low birthweight may themselves represent manifestations of congenital infection, including maternal genital tract infections.

However, it is possible that interventions intended to prevent noncongenital infection deaths during the late neonatal period, and especially the postneonatal period, could be focused on those infants identified at birth as being at increased risk for subsequent infectious disease mortality. Intervention programs that target newborns assessed as being at high risk for infant or postneonatal mortality have been successfully implemented.[32,33] In order to design and implement such intervention programs to decrease infant mortality due to infectious diseases, several questions must be resolved. For example, the association of increased infectious disease mortality risk and factors such as low maternal educational attainment and late initiation of prenatal care suggest that lack of access to health care or improper utilization of the health care system may be important antecedents of infant death. Further insight into the relative importance of access vs utilization of health care requires more specific information about the history of the illness leading to death, information that may be obtainable via systematic review of the medical records of infants who died due to infection during infancy.[34] Infant death reviews should also shed light on other questions, such as (1) What proportion of the infections are nosocomial vs community-acquired? (And, if community-acquired, what proportion are related to attendance at day care?) and (2) What proportion of the infections are vaccine-preventable? (And, if vaccine-preventable, had the infant actually received age-appropriate immunization?)

Finally, with increasing evidence of an association between low birthweight—especially among infants born preterm[30]—and infectious disease mortality during infancy and childhood,[19,28–30] further studies should be performed that distinguish between low birthweight ascribable to preterm birth, intrauterine growth retardation, or both. Such discrimination is important because preventable factors influencing intrauterine growth and length of gestation only partially overlap. □

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