Infectious Disease-Related Deaths of Low Birth Weight Infants, United States, 1968 to 1982

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ABSTRACT. Infant mortality rates in the United States are higher than in any other developed country. Low birth weight (LBW) is the primary determinant of infant mortality. Despite city, state, and federal programs to prevent LBW, decreases in infant mortality in the 1980s appear to be largely secondary to improved survival of LBW infants rather than to a decline in the rate of LBW births. Because prevention of mortality due to infectious disease is feasible, it was of interest to examine the role of infectious diseases in LBW infant mortality. US vital statistics mortality data for 1968 through 1982 were analyzed in terms of LBW infant mortality associated with infectious and noninfectious diseases. These analyses indicated that the rates of infectious disease-associated early neonatal and postneonatal LBW mortality increased during this time; late neonatal rates did not decline appreciably. Infectious diseases were associated with 4% of all LBW infant deaths in 1968; this had increased to 10% by 1982. Although LBW infant mortality rates associated with noninfectious diseases did not differ for white and black populations, infectious disease-associated mortality rates were consistently higher for blacks than whites in both metropolitan and nonmetropolitan areas. Chorioamnionitis was involved in 28% of infectious disease-associated early neonatal LBW deaths. Sepsis was an increasingly listed cause of death in all infant age periods, whereas respiratory tract infections were decreasingly listed. Necrotizing enterocolitis increased as a cause of late neonatal mortality. These data suggest that infectious diseases are an increasing cause of LBW infant mortality and these deaths occur more frequently in the black population targeted by prevention programs. More research concerning specific causes and prevention of infections in the LBW infant may help reduce US infant mortality. *Pediatrics* 1989;84:296-303; *infant mortality, low birth weight, high-risk infant, infectious disease, prematurity.*

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ABBREVIATIONS. LBW, low birth weight; NCHS, National Center for Health Statistics; ICD, *International Classification of Diseases;* VVLBW, very, very low birth weight.

Because infant mortality rates in the United States are higher than those of any other developed country, infant mortality has been called the "central problem of perinatology today."[1] Low birth weight (LBW) is the primary determinant of neonatal (<1 month of age) mortality in this country,[2,3] especially in the black population, for whom the rate is twice that of the white population.[3] Based on these statistics, public health prevention guidelines for the 1980s have targeted a goal of reducing infant mortality rates, especially in ethnic and minority populations with disproportionately high rates,[4] and city, state, and federal programs have been directed toward LBW prevention. Despite these efforts, decreases in infant mortality in this decade appear to be largely secondary to improved survival of LBW infants rather than a decline in the rate of LBW births.[2,3,5-10] Increases in birth weight distribution have been modest at best and have been greater for whites than blacks[2,3,6-9] and for larger infants rather than those of LBW.[9]

Great strides have been made in the first three quarters of this century in preventing infectious disease-related infant mortality.[2,10] In addition, infectious disease-related postneonatal (1 month to <1 year of age) mortality decreased rapidly in the 1960s and 1970s.[10] However, infectious diseases remain an important cause of infant mortality and contributed to nearly 400 000 years of potential life lost by infants in 1980 alone.[11] Furthermore, infectious diseases were the second leading cause of postneonatal mortality for black infants in 1962 to 1978.[10] Infectious disease prevention is both feasible and cost-effective.[11] It was, therefore, of interest

to examine what role infectious diseases might play in LBW infant deaths in the early neonatal (<48 hours of age), late neonatal (48 hours to <1 month of age), and postneonatal periods. Mortality data from the National Center for Health Statistics (NCHS) for 1968 through 1982 were analyzed to examine this issue.

MATERIALS AND METHODS

The NCHS mortality data tapes of all deaths occurring from 1968 through 1982 contain information from all death records received by the NCHS, which are furnished by all 50 states, the District of Columbia, Puerto Rico, the Virgin Islands, and Guam.[12,13] Coding permits a listing of up to 20 causes of death for any person; a cause is to be listed only if it had a direct causative relationship to the person's death (eg, if a person had pneumonia at the time of death but was killed in an accident, pneumonia would not be listed as a cause of death).

Analyses included all infants (<1 year of age at death). For these analyses, death occurring at <48 hours of age is termed an "early neonatal" death; at 48 hours to 27 days, "late neonatal"; and at 28 to 364 days of age, "postneonatal." Data concerning fetal deaths were unavailable for these years and, therefore, were not considered in these analyses.

Cause-of-death coding by the NCHS was based on death certificate information and used the *International Classification of Diseases,* eighth revision (ICD-8) for 1968 through 1978 and the ninth revision (ICD-9) for 1979 through 1982.[14,15] Causes of death were categorized for certification at the NCHS ("record axis coding").[12] This record axis coding was used in these analyses; details have been described previously.[11]

A death was considered related to infectious diseases if any ICD codes indicating an infectious cause were listed as a cause of death, regardless of the rank order in which these were listed. The codes indicating an infectious disease were selected on the basis of two independent reviewers' opinions; disagreements were trivial and did not involve any codes associated with a death. Exact comparability between the ICD-8 and ICD-9 coding was not possible for all cause-of-death categories. Comparable ICD-8 and ICD-9 codes used in some categorizations were based upon consultations with NCHS nosologists. In particular, necrotizing enterocolitis, which is here considered an infectious disease, was coded with gastroenteritis and colitis in ICD-8 and was coded separately in ICD-9. NCHS nosologists indicated that this ICD-8 category represented predominantly necrotizing enterocolitis and not gastroenteritis/colitis.

A death was considered related to LBW if ICD-8 code 777 (prematurity, immaturity, LBW infant) or ICD-9 codes 764.0 to 765.9 (slow fetal growth and fetal malnutrition, including "light for dates," extreme immaturity [birth weight <1000 g and/or gestation of <28 weeks], and disorders relating to short gestation and unspecified LBW) were listed as any cause of death. This provides the best available approximation of US LBW mortality, because national linked birth certificate/death certificate files do not exist for these years. It is unlikely that these codes would be recorded erroneously; however, completeness of recording has yet to be evaluated (K. Praeger, personal communication, NCHS, 1987). To partially assess the degree of LBW misclassification, the relationship between "respiratory distress syndrome" coding (ICD-9 code 769) and LBW coding was examined. Twenty-five percent of deaths coded as involving LBW also involved respiratory distress syndrome compared with 4% of those not coded as LBW; 84% of deaths coded as respiratory distress syndrome associated were also coded as LBW associated. These results were consistent within 2 percentage points for blacks and whites and for metropolitan and nonmetropolitan areas and in 1979 through 1982.

Race- and birth weight-specific data concerning live-born infants for the United States were obtained from the NCHS natality vital statistics (NCHS, unpublished data, 1987).[16] Metropolitan or nonmetropolitan status was defined according to the NCHS and used as a crude index of urbanization for 1969 through 1982. A metropolitan county is a county or group of contiguous counties that contains at least one city of 50 000 inhabitants or more and is socially and economically integrated with the central city.[16] The counties considered metropolitan changed in 1980, a census year, in response to growth of urban centers. Data concerning live-born black infants and for metropolitan/nonmetropolitan areas were unavailable for 1968.

For 1968 through 1978, LBW infant mortality rates were approximated by dividing the number of deaths during that year by the number of live-born infants with birth weights <2500 g (LBW births) for the same year. (Denominator data were unavailable for <2500 g only for those years.) For 1979 through 1982, LBW infant mortality rates were computed by dividing the number of deaths during that year by the number of live-born infants with birth weights <2500 g (LBW births) for the same year. (In 1978, the number of live-born infants <2500 g was 236 342; in 1979, the number of live-born infants <2500 g was 241 826.) Long-term analysis of secular trends should not be greatly affected by these changes or techniques. Late neo-

natal mortality rates were calculated by subtracting the number of LBW early neonatal infant deaths from the denominator of LBW live-born infants; postneonatal mortality rates were calculated by subtracting the number of early and late neonatal LBW infant deaths from the denominator of LBW live-born infants.

RESULTS

General Trends

From 1968 through 1982, the total number of all live-born infants in the United States increased by 5%, from 3 501 564 to 3 680 537. The number of LBW live-born infants declined by 13%, from 286 528 in 1968 to 248 104 in 1982. This reflects a 1% decrease in the percentage of live-born infants who were of LBW, from 8% in 1968 to 7% in 1982. Overall, LBW infant mortality rates declined between 1968 and 1982; the decline for whites was greater than that for blacks (from 130 per 1000 LBW live-born infants in 1969 to 73 per 1000 LBW live-born infants in 1982 for whites compared with from 122 per 1000 LBW live-born infants in 1969 to 79 per 1000 LBW live-born infants in 1982 for blacks [live-born infant data for blacks and metropolitan/nonmetropolitan areas were unavailable for 1968]). Infectious diseases were associated with 4% of LBW infant deaths in 1968; this proportion increased to 10% by 1982. Infectious disease-related LBW infant mortality rates increased from 5.3 per 1000 LBW live-born infants in 1968 to 7.1 per 1000 LBW live-born infants in 1982.

ICD-9 coding enables specification of deaths recorded as being of infants <1000 g and/or gestation <28 weeks (very very LBW, VVLBW). For 1979 through 1982, the proportion of LBW infant deaths involving VVLBW infants increased from 36% to 43% of all LBW infant deaths; this proportionate increase was true for both infectious disease-related (17% of LBW infant deaths were of VVLBW infants in 1979; this increased to 27% in 1982) and noninfectious disease-related (increasing from 35% to 45%) LBW infant deaths. The estimated overall VVLBW infant mortality rate increased slightly during this 4-year period, from 360 per 1000 to 380 per 1000; the rate for those with birth weights >1000 g but <2500 g declined slightly, from 59 per 1000 to 46 per 1000. In 1979, the infectious disease-related VVLBW infant mortality rate was 2.5 times that of other LBW infants; by 1982, it was 4.1 times that of other LBW infants. In 1979, the noninfectious disease-related VVLBW infant mortality rate was 6.5 times that of other LBW infants; this had increased to 8.8 times by 1982. The proportion of LBW infant deaths that were related to infectious diseases increased for both VVLBW infants (4.5% to 6.2%> and other LBW infants (10.6% to 12.4%) during this 4-year period. In each year, infectious disease-related LBW infant mortality rates were higher for blacks than whites. Rates for both races increased until 1976 and then declined slightly until 1979. Rates for white infants were stable between 1980 and 1982; rates for black infants increased from 7.5 per 1000 LBW live-born in 1980 to 8.4 per 1000 LBW live-born in 1982.

Metropolitan/Nonmetropolitan Areas

From 1969 through 1982, the total number of metropolitan live-born infants increased by 18%, from 2 351 108 to 2 767 113, whereas the total number of nonmetropolitan live-born infants declined by 27%, from 1 249 098 to 913 424. The number of metropolitan LBW live-born infants declined by 3%, from 195 470 to 188 964 and the number of nonmetropolitan LBW live-born infants declined by 37%, from 94 458 to 59 140. This reflects a 1% decrease in the proportion of metropolitan live-born infants who were of LBW (8% to 7%) and a 2% decrease in the proportion of nonmetropolitan live-born infants who were of LBW (8% to 6%). Infectious disease-related LBW infant mortality rates increased until 1976 in both metropolitan and nonmetropolitan areas, declined, and then increased again in 1982. In all but 4 years, metropolitan rates exceeded nometropolitan rates (in 1982, 7.3 per 1000 LBW live-born infants vs 6.7 per 1000 LBW live-born infants); nonmetropolitan rates exceeded metropolitan rates in 1970 (6.2 per 1000 LBW live-born infants vs 5.7 per 1000 LBW live-born infants) and 1976 (8.2 per 1000 LBW live-born infants vs 8.1 per 1000 LBW live-born infants). Metropolitan rates for white infants exceeded nometropolitan rates in all but 3 years; nonmetropolitan rates for black infants exceeded metropolitan rates in 4 years (Fig 1). Rates for black infants exceeded those for white in both metropolitan and nonmetropolitan areas in every year (Fig 1).

Early Neonatal, Late Neonatal, and Postneonatal Mortality

During this period, 71% of early neonatal deaths, 44% of late neonatal deaths, and 5% of postneonatal deaths were accounted for by LBW infants. The proportion of LBW infant deaths that occurred in the early neonatal period declined from 81% in 1968 to 71% in 1981 and increased to 73% in 1982 (76% overall, n = 293 878). The proportion occurring in the late neonatal period increased from 18% in 1968 to 24% in 1981 and declined to 21% in 1982

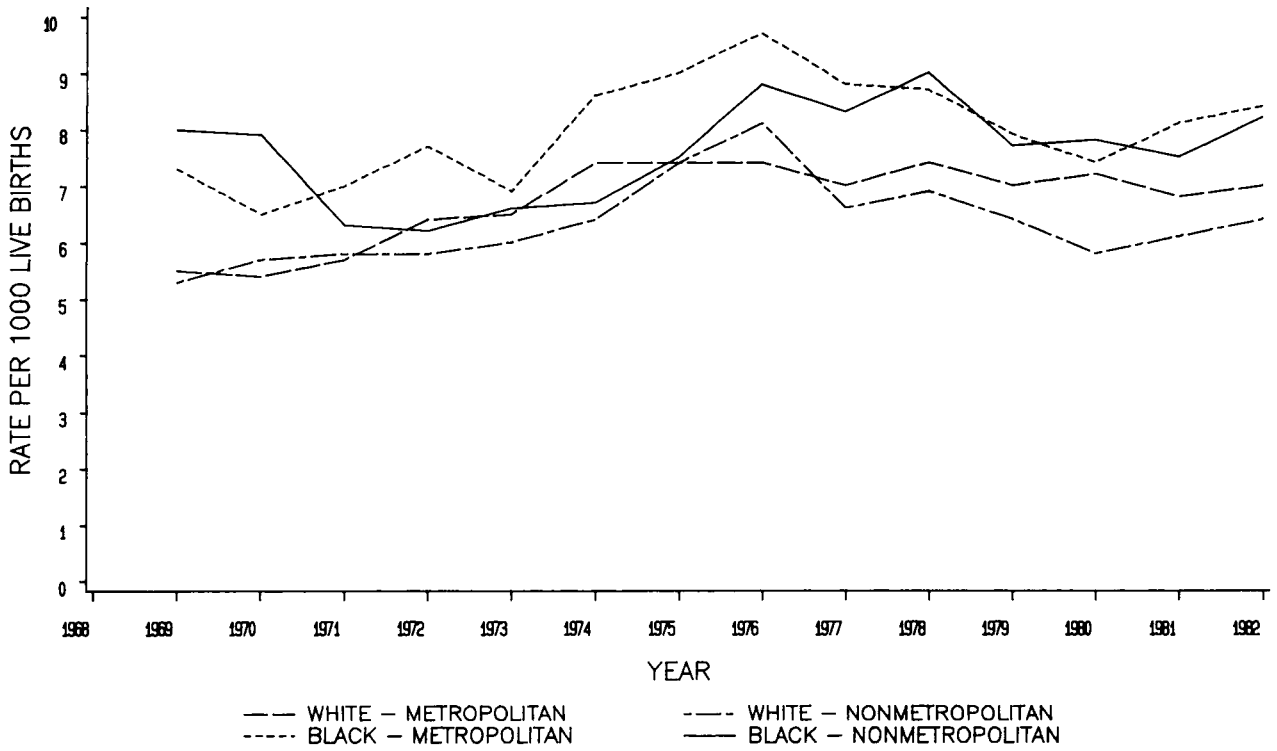

Fig 1. Rates of low birth weight mortality associated with infectious diseases, by race, metropolitan status, and year; United States, 1969 through 1982. (Data are unavailable concerning number of live births in US black population and broken into metropolitan status in 1968.)

(21% overall, n = 82 597). The proportion that occurred in the postneonatal period increased from 1% in 1968 to 6% in 1982 (3% overall, n = 10 993).

Infectious diseases were recorded in fewer than 6% of early neonatal LBW infant deaths. However, whereas overall LBW early neonatal mortality rates declined markedly between 1968 and 1982 (from 102.5 per 1000 LBW live-born infants to 53.8), mortality associated with infectious diseases increased (from 1.8 per 1000 LBW live-born infants to 2.9). Rates for white and black infants differed by <0.5 per 1000 LBW live-born infants in each year. Noninfectious disease-associated LBW late neonatal mortality rates also declined markedly in the second half of this period (from a peak of 22.4 per 1000 LBW live-born infants in 1974 to 13.1 in 1982); infectious disease-associated LBW late neonatal mortality rates did not (3.1 per 1000 LBW live-born infants in 1968 and 2.9 in 1982). Noninfectious disease-associated LBW late neonatal mortality rates for blacks were higher than those for whites, but this racial difference declined in 1981 and 1982. Infectious disease-associated LBW late neonatal mortality rates for blacks were higher than those for whites in all but one year (eg, in 1982, 3.6 per 1000 LBW live-born infants vs 2.7 per 1000 LBW live-born infants). Infectious disease-related deaths were a major component of LBW postneonatal mortality for both white and black babies (Fig 2). Noninfectious disease-associated LBW postneonatal mortality rates increased more than twofold from 1.4 per 1000 LBW live-born infants in 1968 to 3.0 per 1000 LBW live-born infants in 1982. (Deaths coded as "sudden death" [ICD-9 798], including "sudden infant death syndrome" [ICD-9 798.0], constituted a large proportion of this increase.) Rates of infectious disease-related LBW postneonatal mortality also increased during this period, from 1.1 per 1000 LBW live-born infants in 1968 to 1.6 per 1000 LBW live-born infants in 1982; rates for blacks were consistently higher than those for whites.

Types of Infectious Diseases

The infectious diseases associated with LBW infant mortality changed during this period. Changes in ICD coding in 1979 might have influenced some of these recorded trends, but sudden changes were not seen between 1978 and 1979 (Fig 3). Respiratory tract infections decreased markedly as a recorded cause of infectious disease-associated death (from 887 deaths in 1968 to 207 in 1982). Conversely, chorioamnionitis and sepsis were increasingly recorded as causes of infant mortality (from 146 deaths in 1968 to 273 in 1982 and from 362 deaths in 1968 to 1007 in 1982, respectively). Necrotizing enterocolitis and brain infections

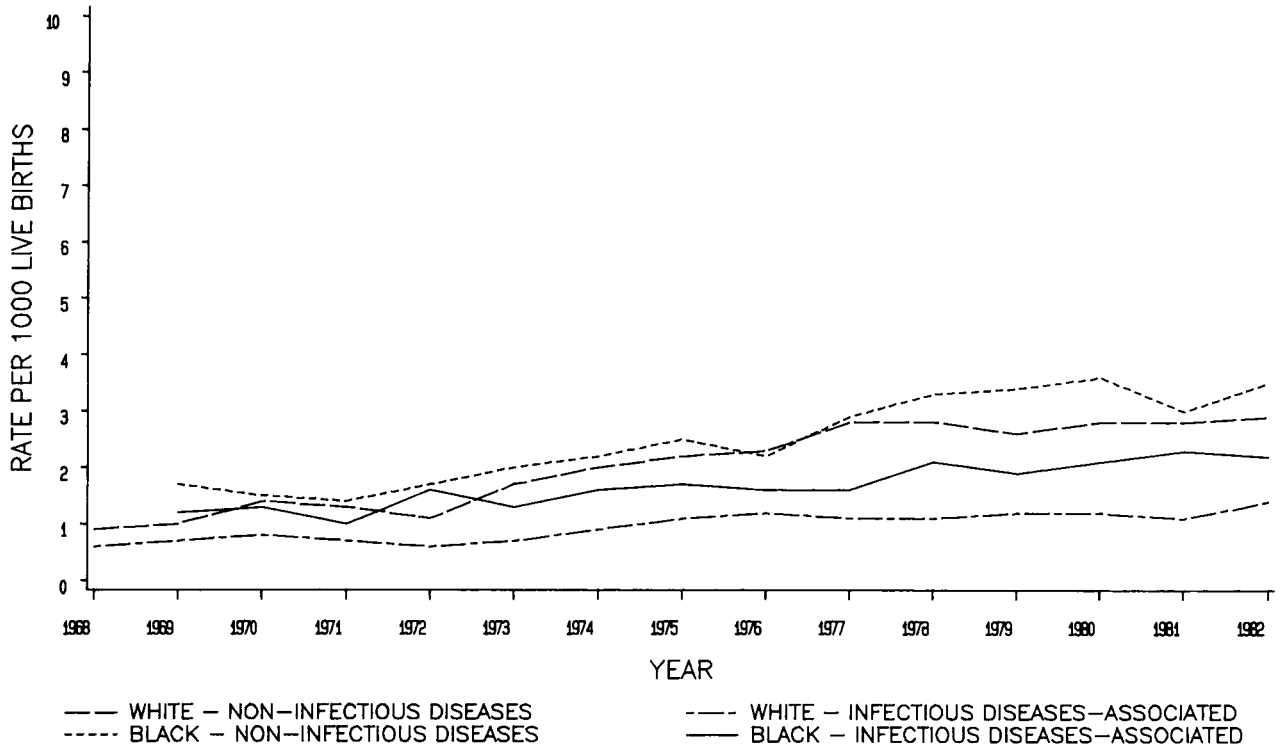

Fig 2. Rates of low birth weight postneonatal mortality, by association with infectious diseases, race, and year; United States, 1968 through 1982. (Data are unavailable concerning number of live births in US black population in 1968.)

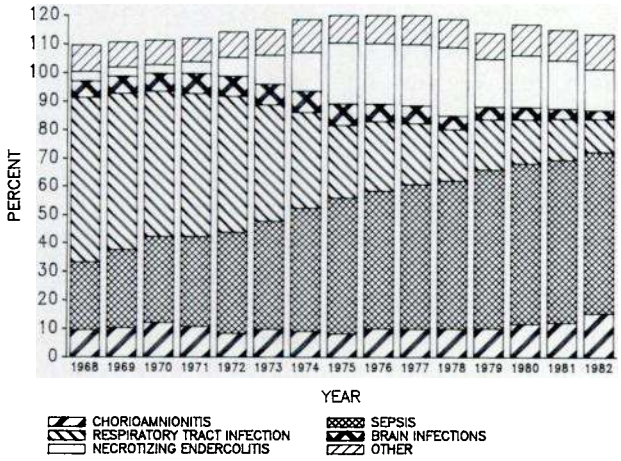

Fig 3. Proportion of infectious disease-associated low birth weight infant deaths associated with specific infectious diseases; United States, 1968 through 1982. (Totals exceed 100% because a given death may have been associated with more than one infectious disease.)

peaked as causes of infectious disease-associated infant mortality in 1975 through 1978 and 1974 through 1975, respectively, and have since declined. These patterns were similar for white and black infants, although whites had a lower overall proportion of necrotizing enterocolitis-associated deaths (2033 [12%] vs 1338 [16%]).

The infectious diseases associated with LBW infant deaths differed for the three age periods (Table). Chorioamnionitis was listed in 28% of infectious-disease associated early neonatal LBW infant deaths but was rarely listed for the later age periods. Sepsis was a major and increasing cause of LBW infant death for all three age periods. In 1968, sepsis was associated with 18% of infectious disease-associated early neonatal, 29% of infectious disease-associated late neonatal, and 16% of infectious disease-associated postneonatal deaths. By 1982, these figures had increased to 60%, 59%, and 48%, respectively. The organism causing sepsis was specified 10% of the time. Respiratory tract infections declined as an infectious disease-associated cause of death in all three age periods, by 45 percentile points in the early neonatal and late neonatal periods and by 54 percentile points in the postneonatal period (from 71% in 1968 to 17% in 1982). Necrotizing enterocolitis was rarely diagnosed in the early neonatal period but increased as a proportionate cause of infectious disease-associated late neonatal death through 1980 (from 4% in 1968 to 37% in 1980) and then declined slightly, to 33% in 1982. ICD-coding changes seem to have most affected the coding of necrotizing enterocolitis for postneonatal deaths. Necrotizing enterocolitis was associated with 8% of infectious disease-associated postneonatal deaths in 1968. This increased to 37% in 1978, declined to 9% in 1979, again increased to 15% in 1981, and declined to 10% in

TABLE. Infectious Disease-Associated Low Birth Weight Infant Deaths by Specific Infectious Diseases and Age Period, United States, 1968 Through 1982*

Cause of Death	% of Early Neonatal Deaths (n = 8891)	% of Late Neonatal Deaths (n = 12 758)	% of Postneonatal (n = 3902)
Chorioamnionitis	28	1	<1
Sepsis	44	47	35
Respiratory tract infection	29	32	40
Brain infection	2	8	8
Necrotizing enterocolitis	<1	22	17
Other	5	10	21

* Totals may exceed 100% because a given death may have been associated with more than one infectious disease.

1982. Other infectious causes were decreasingly recorded for the early and late neonatal periods during this time period. However, as with necrotizing enterocolitis and probably related to necrotizing enterocolitis-coding changes, ICD-9 code revisions appear to have affected the postneonatal coding of "other." In 1978, 13% of postneonatal infectious disease-associated LBW infant deaths listed this category; in 1979, this figure increased to 26% and continued to increase in subsequent years, to 40%. The category "other" includes intestinal infections other than necrotizing enterocolitis. In 1979, 15% of infectious disease-related postneonatal mortality was associated with nonnecrotizing enterocolitis intestinal infection; this had increased to 23% by 1982. Similar figures cannot be derived using ICD-8 coding.

DISCUSSION

Results of this study suggest that the rate of infectious disease-associated LBW infant mortality has increased, although the total number of LBW births and overall LBW infant mortality rate have declined. This is especially worrisome because infectious diseases are a potentially preventable cause of infant death. The increase was seen for both metropolitan and nonmetropolitan areas. Furthermore, infectious disease-associated infant mortality rates were consistently higher for blacks, despite the targeting of public health prevention projects toward this at-risk population.[4]

The data from this study are limited by both the method used in estimating LBW infant deaths (ie, ICD coding of LBW) and the amount, accuracy, and detail available from vital statistics. Other than the respiratory distress syndrome calculation described in "Materials and Methods," there is currently no way to further assess the accuracy and completeness of ICD LBW coding; further assessment will eventually be possible using linked birth certificate/death certificate files now being developed at the NCHS (K. Praeger, personal communication, NCHS, 1987). Despite this limitation, these analyses are important because they are the only feasible way to examine US LBW infant mortality trends during a recent 15-year period. These data, if varified by further studies, suggest that infectious diseases should be targeted to prevent LBW infant mortality. Furthermore, these results can be used to direct more in-depth, medical record-based studies oriented toward race- and age-specific LBW mortality.

Targeting of infectious diseases may be worthwhile for all infant age groups. Noninfectious disease-associated early and late neonatal mortality rates declined markedly, but infectious disease-associated mortality rates did not. Late neonatal mortality rates for blacks were variable but increased between 1979 and 1982. Furthermore, except for chorioamnionitis, these findings do not reflect maternal infections that may cause preterm birth and, secondarily, early and late neonatal mortality[17-20]; thus, they are a minimum estimate of the role of infection in early and late neonatal deaths. These analyses also indicate that infectious diseases are a major and increasing cause of postneonatal mortality for both white and black LBW infants. Most important, especially in terms of prevention targeting, is the finding that infectious disease-associated infant mortality rates for blacks exceeded those for whites in the late neonatal and postneonatal periods, despite the lack of a racial difference in early neonatal mortality rates. Further study is needed to determine whether this reflects differences in access to or quality of medical care, which are thought to be factors in LBW births,[21] and whether, in addition, it reflects differences in the speed of parental recognition of an infant's need for medical care after the infant has left the hospital newborn nursery.

Changes in specific causes of infectious disease-associated death also provide directions for future research. First, more in-depth studies are needed to determine whether trends reflect changes in any or all of the following: criteria for diagnosis, disease

recording, disease occurrence, or mortality associated with a disease category. For example, the decline in mortality associated with respiratory tract infection may reflect real improvements in the medical care of a LBW infant with significant pulmonary problems. It may also reflect a decreasing inclination to classify deaths of uncertain cause as being due to a pulmonary infection. A diagnosis of sepsis is frequently made on clinical, rather than laboratory, criteria. Only a small portion of ICD-coded cases of sepsis had a specific organism listed; this proportion did not increase during this time. It cannot be ascertained whether this reflects an absence of laboratory confirmation of sepsis or a failure to note on the death certificate records the organisms involved. Similarly, chorioamnionitis may be diagnosed using clinical and/or histologic criteria. ICD coding does not permit a determination of the criteria used in recorded cases of chorioamnionitis. Necrotizing enterocolitis appears to be an emerging late neonatal problem; however, postneonatal necrotizing enterocolitis trends are difficult to assess because of ICD-8 to ICD-9 coding changes. In ICD-8, necrotizing enterocolitis could not be distinguished from "gastroenteritis and colitis"; in ICD-9, necrotizing enterocolitis is clearly differentiated. A diagnosis of "necrotizing enterocolitis" should be based on firm clinical and radiologic criteria[22]; therefore, the large 1978 to 1979 change in proportion of infectious disease-associated postneonatal deaths associated with necrotizing enterocolitis suggests that some LBW postneonatal deaths occurring before 1979, which we have here considered necrotizing enterocolitis associated (based on personal communications with NCHS nosologists, 1987), were, in fact, related to gastroenteritis, not necrotizing enterocolitis. This does not appear to be the case with late neonatal deaths recorded as necrotizing enterocolitis, for which the 1978 to 1979 change is unremarkable. Further investigation of this issue, using medical record-based data, would be useful, especially because gastroenteritis is an easily preventable cause of mortality.

To varying degrees, age-specific trends in infectious disease-associated LBW infant mortality may reflect interactive medical, biologic, and social factors that influence both LBW infant survival and risk of infection. These factors include (1) the escalating sophistication of medical intensive care technology, (2) the immunologic deficiencies of the LBW newborn, and (3) the increased use of nonhome day-care facilities. Each of these merits evaluation to determine its effects on the age distribution, rate, and specific causes of LBW infant mortality.

LBW infant survival has improved because of the widely disseminated availability of neonatal intensive care units and neonatal intensive care unit technology.[23] However, this improvement has not been without costs, including the increasing risk of a neonatal intensive care unit patient acquiring one or more nosocomial infections. In an estimated 25% of infants treated in neonatal intensive care units, a nosocomial infection develops, and nearly a third of these die.[24] These deaths usually occur in the late neonatal period but can occur much later. Their contribution to infant mortality should be further investigated. An increased emphasis on developing neonatal intensive care unit prevention/infection-control measures may be warranted.

LBW survivors have greater and more prolonged immune deficiencies than do full-term, normal birth weight infants; the degree and duration of these deficiencies vary inversely with gestational age and birth weight. Analyses using ICD-9 coding suggest that infants of birth weights <1000 g and/or very short gestation (<28 weeks) represent an increasing proportion of LBW infant deaths. The mortality rate for these infants increased between 1979 and 1982; the mortality rate for those >1000 g but <2500 g declined slightly. However, an increasing proportion of deaths in both weight groups were associated with infectious diseases. These findings support the idea that, as early neonatal survival improves, immune deficiencies may be increasingly important factors in late neonatal and postneonatal survival. These deficiencies influence the LBW infant's response to infections in both hospital and community settings. The increasing contribution of sepsis to LBW infant mortality in all three age periods may reflect the susceptibility of the LBW infant to infection, both at birth and after the early neonatal period. The relative risks of nosocomially and community-acquired infections of LBW infants surviving the early neonatal period should be investigated. Furthermore, the effect of recent and ongoing advances in medical care, eg, the use of intravenous α-globulin for infected neonates[25,26] and maternal antibiotic therapy,[27] on early and late neonatal mortality rates is unknown. Finally, the mortality risk for a LBW infant cared for in a nonhome day-care facility, as compared with a LBW infant cared for at home, warrants evaluation. The expanding female work force has lead to increasing use of day-care facilities for young infants; the women most likely to have LBW infants are those least likely to be able to afford home child care. The transmission of infectious diseases within these facilities may affect LBW infant morbidity and mortality.[28-30]

IMPLICATIONS

In conclusion, infectious diseases are potentially preventable causes of LBW infant mortality. Rates of infectious disease-associated early neonatal and postneonatal mortality may be increasing; late neonatal rates do not appear to be declining appreciably. These trends suggest that more active research is needed concerning specific causes and prevention of infectious disease-associated LBW infant death.

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REFERENCES

1. Lontos J. Baby Doe five years later: implications for child health. *N Engl J Med.* 1987;317:444–447
2. McCormick MC. The contribution of low birthweight to infant mortality and childhood morbidity. *N Engl J Med.* 1985;312:82–90
3. Williams RL, Chen PM. Identifying the sources of the recent decline in perinatal mortality rates in California. *N Engl J Med.* 1982;306:207–214
4. Wolnez GJ, Wolverton S, Woteki C, Yarber WL, Young EA, Zifferblatt S. *Promoting Health/Preventing Disease. Objectives for the Nation.* Washington, DC: US Department of Health and Human Services, Public Health Service publication 349–256; 1980
5. Lee KS, Paneth N, Gartner LM, et al. Neonatal mortality: an analysis of the recent improvement in the United States. *Am J Public Health.* 1980;70:15–21
6. Buehler JW, Kleinman JC, Hogue CJR, et al. Birthweight-specific infant mortality, United States, 1960 and 1980. *Public Health Rep.* 1987;102:151–161
7. Kleinman JC, Kesal SS. Racial differences in low birth weight: trends and risk factors. *N Engl J Med.* 1987;317:749–753
8. David RJ, Siegel E. Decline in neonatal mortality, 1968 to 1977: better babies or better care? *Pediatrics.* 1983;71:531–540
9. Goldenberg RL, Humphrey JL, Hale CB, et al. Neonatal deaths in Alabama, 1970–1980, an analysis of birth weight- and race-specific neonatal mortality rates. *Am J Obstet Gynecol.* 1983;145:545–552
10. Khoury MJ, Erickson JD, Adams MJ Jr. Trends in postneonatal mortality in the United States 1962 through 1978. *JAMA.* 1984;252:367–372
11. Jason JM, Jarvis WR. Infectious diseases: preventable causes of infant mortality. *Pediatrics.* 1987;80:335–341
12. National Center for Health Statistics. *Public Use Data Tape Documentation. Multiple Cause of Death for ICD-9 1980 Data.* Hyattsville, MD: US Dept of Health and Human Services; 1983
13. National Center for Health Statistics. *Instruction Manual, part 2f: ICD-9 Transax Disease Reference Tables for Classifying Multiple Causes of Death, 1979–1980.* Hyattsville, MD: US Dept of Health and Human Services; 1983
14. National Center for Health Statistics. *Eighth Revision International Classification of Diseases.* Adapted for use in the United States. Washington, DC: US Dept of Health, Education, and Welfare publication (PHS) 1963; 1968
15. World Health Organization. *Manual of the International Statistical Classification of Diseases, Injuries, and Causes of Death.* Based on the recommendations of the ninth revision conference, 1975 and adopted by the 29th World Health Assembly. Geneva, Switzerland: World Health Organization; 1977.
16. National Office of Vital Statistics. *Vital Statistics of the United States. I: Natality.* Editions for 1968 through 1982. Hyattsville, MD: National Center for Health Statistics, US Dept of Health and Human Services; 1970–1986
17. Quinn PA. Evidence of an immune response to *Ureaplasma urealyticum* in perinatal morbidity and mortality. *Pediatr Infect Dis* 1986;5:S282–287
18. Berman SM, Harrison HR, Boyce WT, et al. Low birthweight, prematurity, and post partum endometritis: association with prenatal cervical *Mycoplasma hominis* and *Chlamydia trachomatis* infections. *JAMA.* 1987;257:1189–1194
19. Guzick DS, Winn K. The association of cxhorioamnionitis with preterm delivery. *Obstet Gynecol.* 1985;65:11–16
20. Quinn PA, Butany J, Taylor J, Hannah W. Chorioamnionitis: its association with pregnancy outcome and microbial infection. *Am J Obstet Gynecol.* 1987:156:379–387
21. Eisenberg L. Preventive pediatrics: the promise and the peril. *Pediatrics.* 1987;80:415–422
22. Gaynes RP, Palmer S, Martone WJ, et al. The role of host factors in an outbreak of necrotizing enterocolitis. *Am J Dis Child.* 1984;138:1118–1120
23. Kitchen WH, Campbell DG. Controlled trial of intensive care for very low birth weight infants. *Pediatrics.* 1971;48:711–714
24. Hemming VG, Overall JC Jr, Britt MR. Nosocomial infections in a newborn intensive care unit. *N Engl J Med.* 1976;294:1310–1316
25. Haque KN, Zaidi MH, Haque SK, et al. Intravenous immunoglobulin for prevention of sepsis in preterm and low birthweight infants. *Pediatr Infect Dis.* 1986;5:622–625
26. Chirico G, Rondini G, Plebani A, et al. Intravenous immunoglobulin therapy for prophylaxis of infection in high-risk neonates. *J Pediatr.* 1987;110:437–442
27. Boyer KM, Gotoff SP. Presentation of early-onset neonatal group B streptococcal disease with selective intrapartum chemoprophylaxis. *N Engl J Med.* 1986;314:1665–1669
28. The Child Day-Care Infectious Disease Study Group. Public health considerations of infectious diseases in child day-care centers. *J Pediatr.* 1984;105:683–701
29. Bartlett AV, Moore M, Gary GW, et al. Diarrheal illness among infants and toddlers in day-care centers, II: comparison with day-care homes and households. *J Pediatr.* 1985;107:503–509
30. Istre G, Conner J, Broome CV, Hightower A, Hopkins R. Risk factors for primary invasive *Haemophilus influenzae* disease: increased risk from day-care attendance and school-aged household members. *J Pediatr.* 1985;106:190–195

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