Infectious Diseases: Preventable Causes of Infant Mortality

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ABSTRACT. After almost a century of improvement, the rate of decrease in US infant mortality rates began to level off during the period of 1982 to 1984. Rates actually increased in some states. Because much of the decline in infant mortality in this century can be attributed to advances in infectious disease treatment and prevention programs, we evaluated the current impact of infectious diseases on infant mortality. The National Center for Health Statistics mortality data for 1980 contains information on as many as 20 causes of death for a given individual. Using these data, we found that infectious diseases contributed to 12.5% of all infant deaths and to almost 400,000 years of potential life lost because of infant deaths. Infectious diseases contributed to 9% of deaths of low birth weight infants and to more than 18% of all deaths in the postneonatal period. Compared with white infants, a higher proportion of nonwhite infants died of causes related to infectious diseases. For black infants, the mortality rate related to infectious diseases was twice that for white infants. These data indicate that infectious diseases still are a major contributor to infant mortality, one of the 15 areas targeted for prevention by the federal government, and the data suggest that programs for reducing infant mortality should place increased emphasis on preventing infectious diseases. *Pediatrics* 1987;80:335–341; *infant mortality, low birth weight infant, infectious disease, birth defect.*

Infant mortality trends are considered to be a barometer of technologic advancement and have been linked to the quality of infant and maternal care, nutrition, sanitation, and medical technology.[1-5] Therefore, these trends have induced the development and orientation of social programs and have become tacit indicators of a nation's quality of life.[3,5,6] Infant mortality rates in industrialized countries declined rapidly in the first three quarters of this century.[1,3,4,7,8] During the period of 1915 to 1970, the decline in infant mortality was greater for postneonatal mortality (defined as death of infants 1 to 11 months of age) than for neonatal mortality (defined as death of infants less than 1 month of age). This decline is attributed to improved nutrition and a reduction in infectious disease-related mortality.[1,4,7,8] This pattern changed after 1970, with neonatal mortality declining faster than postneonatal mortality.[3,9] In fact, between 1983 and 1984, US infant mortality rates began to level off and, although neonatal mortality rates continued to decline, postneonatal rates have increased.[5]

Preventable causes of postneonatal mortality are largely infectious diseases.[1,4,7] Although low birth weight (defined as weight of < 2,500 g at birth) is the most important determinant of neonatal mortality,[3,4,6] infectious diseases may contribute more to perinatal mortality (defined as death of infants less than 48 hours of age) than is reflected in vital statistics data.[10] Discussions and programs oriented toward reducing infant mortality have concentrated on preventing low birth weight and have been oriented toward high-risk groups, especially the black population, whose infant mortality rate is more than three times, and rate of low birth weight births is more than twice, that of white population.[3,4,6,11] Despite this orientation, the decline in infant mortality in the 1970s reflected an increased survival of low birth weight infants, not a reduction in the proportion of low birth weight births.[4,9,12] Prenatal maternal behaviors, especially smoking and alcohol use, are thought to be related to infant birth weight; many low birth weight prevention programs are oriented toward modifying these behaviors. However, such programs have not been found to be effective to date.[5] Furthermore, racial differences in infant mortality cannot be attributed to differences in maternal smoking and alcohol use.[13] In

Received for publication Oct 27, 1986; accepted Nov 20, 1986.
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contrast, many infectious diseases can be prevented, and their prevention has had a remarkable effect upon infant mortality in this century.[14–20] Also, infectious diseases are a relatively more important determinant of mortality and morbidity among socioeconomically deprived populations targeted for infant mortality prevention.[1,6,8]

We believed that an evaluation of US infant mortality data would be useful as a first step in (1) determining the proportion of deaths caused by infectious diseases, (2) identifying the infectious diseases that cause infant deaths, and (3) suggesting to policymakers which infectious diseases might be priority prevention areas in the future. To accomplish this first step, we used the 1980 National Center for Health Statistics (NCHS) mortality data tape, which lists as many as 20 causes of death for any given individual, to evaluate the role of infectious diseases in national infant mortality.

MATERIALS AND METHODS

The NCHS mortality data tape of all deaths occurring in 1980 contains information from all death records received by NCHS, which are furnished by all states, the District of Columbia, Puerto Rico, the Virgin Islands, and Guam.[21,22] Coding permits a listing of as many as 20 causes of death for any individual. In theory, nothing is listed as a cause unless it had a direct causative relationship to that individual's death (eg, if an individual had pneumonia at the time of death but was killed in an accident, pneumonia would not be listed as a cause of death). Cause-of-death coding by NCHS was based on death certificate information and used the *International Classification of Diseases, Revision 9* (ICD–9).[23] Causes of death were codified by NCHS in two separate ways[21, 22] The first method of coding causes of death was entity axis coding, in which causes were ranked in the order that they were listed on the death certificate, without linkage to any other listed cause. (NCHS,[21] states that "this coding is not conducive to the generation of person-based multiple cause statistics.") The second method of coding causes of death was record axis coding, in which causes were linked into the most meaningful categories for certification by NCHS. (NCHS[21] states that "in contrast to entity axis data, record axis data are classified in a manner comparable to underlying cause-of-death classification, thereby facilitating joint analysis of these variables." The process of coding is as follows:[24]

All codes (as many as 20 per certificate) are entered into an "entity axis" in the order in which they appear on the certificate. A computer program (TRANSAX) examines the cluster of codes, resolving ambiguities, discards or adds codes as appropriate, and rewrites the codes to a second grouping, the "record axis." The record axis is then examined by another computer program (ACME), which determines the underlying cause of death and adds it to the record. In principle, the underlying cause of death should be on the record axis as well. When ACME cannot make a determination, the certificate is passed to a nosologist, who determines the underlying cause of death and adds it to the record axis if it is not already there.

In our analyses, we used record axis codes for all but rank order analyses; however, results were nearly identical when entity axis codes were used. For example, 12.6% of deaths were related to infectious diseases when entity axis codes were used, and 12.5% of deaths were related to infectious diseases when record axis codes were used. Information about causes of death as listed on the death certificate is based on entity axis codes.[21,22] Data were included for all individuals younger than 1 year of age at the time of death. For these analyses, a death occurring before 48 hours of age is termed "perinatal"; a death occurring at 48 hours to 27 days of age is termed "neonatal"; and a death occurring at 28 to 364 days of age is termed "postneonatal." A death was considered to be related to infectious diseases if any of the ICD-9 codes given in Table 1 were listed as any cause of death, regardless of the rank order in which it was listed. Some of the codes did not have any deaths associated with them. "Minimal-risk infants" were defined as those without the following codes listed as any cause of death: 764.0 or 764.1 ("light-for-dates"), 764.9 ("fetal growth retardation"), 765.0 to 765.1 ("extreme immaturity" and "other preterm infants"), and 740.0 to 759.0 ("congenital abnormalities"). Individuals with codes 764.0, 764.1, 764.9, or 765.0 to 765.1 listed as any cause of death will be referred to as "low birth weight." Individuals with codes 740.0 to 759.0 listed as any cause of death will be referred to as infants with "congenital defects." Those coded as having low birth weight and/or congenital defects and/or infectious diseases will be included in each of the multiple categories, where percentage distributions are given. Data on live births for US regions and races were obtained from NCHS vital statistics.[25] Regional data are based on place of residence. Years of potential life lost before 65 years of age were calculated as follows: $T(65 - [A/365.25])$, where A = the median age at death in days for each age group and T = the total number of infectious disease-related deaths in that age group.

RESULTS

Infectious diseases were recorded as causes of

TABLE 1. International Classification of Diseases, Ninth Edition, Codes Related to Infectious Diseases

Code No.	Description
001–139	Infectious and parasitic diseases
320.0–321.8	Meningitis: bacterial or due to other organisms
323.0–323.4	Encephalitis: viral, rickettsial, protozoal, or infection classified elsewhere
324	Intracranial or intraspinal abscess
372.2–372.3	Conjunctivitis
373.4–373.6	Eyelid infection
420	Acute pericarditis
421.0–421.1	Infective endocarditis
422	Acute myocarditis
460	Acute nasopharyngitis
462	Acute pharyngitis
463	Acute tonsillitis
464	Acute laryngitis and tracheitis
465.0–465.9	Acute upper respiratory infections of multiple or unspecified sites
466	Acute bronchitis and bronchiolitis
480.0–484.8	Pneumonia: viral, bacterial, due to other specified agents
485	Bronchopneumonia
486	Pneumonia
487	Influenza
510	Empyema
511.0–511.1	Pleurisy
513	Abscess of lung and mediastinum
566.0	Abscess of anal and rectal regions
567	Peritonitis
569.5	Intestinal abscess
572.0	Liver abscess
590.0–590.9	Kidney infection
762.7	Chorioamnionitis
770.0	Congenital pneumonia
771.0–771.8	Infections specific to the perinatal period
777.5	Necrotizing enterocolitis in fetus or newborn
996.6	Infection associated with an internal graft or implant
998.5	Postoperative infection
999.0	Generalized vaccinia
999.3	Other infection following infusion, injection, transfusion, or vaccination

death for 12.5% of all infant deaths (Table 2). In entity axis coding, 4.7% of infants had an infectious disease as the first-listed (immediate) cause of death, 12.4% had an infectious disease listed as one of the first five causes of death, and 12.6% had an infectious disease listed as one of the first ten causes of death. Infectious diseases contributed to as much as 18.2% of deaths in the postneonatal period. In total, 369,730 years of potential life were lost in 1980 because of infectious disease-related infant deaths. The proportion of deaths related to infectious diseases was higher for black than for white infants and highest for the "other" category (Table 3). Although the incidence of congenital defects-related deaths was comparable for white and black infants, the rates of both low birth weight and infectious diseases-related mortality were more than twice as high for black infants (Table 4).

TABLE 2. Proportion of 45,600 Infant Deaths Related or Not Related to Infectious Diseases, by Age Group in the United States, 1980

	Relation to Infectious Diseases (%)	
	Associated (n = 5,702)	Not Associated (n = 39,898)
Perinatal (n = 19,641)	5.7	94.3
Neonatal (n = 11,017)	17.0	83.0
Postneonatal		
28 d–3 mo (n = 8,855)	17.1	82.9
4–6 mo (n = 3,546)	17.8	82.2
7–9 mo (n = 1,745)	22.3	77.7
10–11 mo (n = 796)	22.6	77.4
Total	12.5	87.5

TABLE 3. Proportion of Infant Deaths Related to Infectious Diseases, by Race, United States, 1980

	Race (%)		
	White (n = 31,928)	Black (n = 12,615)	Other (n = 1,057)
Infectious diseases (n = 5,702)	11.9	13.7	14.9
Noninfectious diseases (n = 39,898)	88.1	86.3	85.1

A congenital defect was listed as a cause of death in 21.3% of all infant deaths; low birth weight was listed in 42.9% of these deaths. The contribution of low birth weight was greatest in the perinatal period and declined rapidly thereafter. The contribution of congenital defects was greatest in the neonatal period (Fig 1). Infectious diseases contributed to infant deaths in both the neonatal and postnatal period. The largest number of infectious disease-related deaths occurred in the 11-month postneonatal period (n = 2,716). Among low birth weight infants who died, 7% had a congenital defect and 9% had an infectious disease.

Infectious disease-related deaths were associated with 109,270 years of potential life lost to low birth weight infants. However, the proportion of deaths related to infectious diseases was greatest for infants of normal birth weight without congenital defects (ie, minimal-risk infants) (Fig 2). For infants with low birth weight or congenital defects, infectious disease became a more important cause of infant mortality as these children grew older and moved through the perinatal, neonatal, and postneonatal periods (Fig 3). For minimal-risk infants, infectious diseases predominated as a cause of death in the neonatal period.

TABLE 4. Infant Mortality Rates, by Race and Relation to Infectious Diseases, Low Birth Weight, or Congenital Defects, United States, 1980*

Category	Race			Total (N = 45,600)
	White (n = 31,928)	Black (n = 12,615)	Other (n = 1,057)	
Infectious diseases	1.3	2.9	1.3	1.6
Low birth wt†	4.5	10.4	3.0	5.4
Congenital defects	2.7	2.9	2.0	2.7
Total mortality	11.0	21.4	8.5	12.5

* Results are expressed per 1,000 live births. The categories are not mutually exclusive.
† If infants with birth weights <2,500 g are used as the denominator,[25] mortality would be 79.2 per 1,000 low birth weight live births for white infants and 83.3 per 1,000 low birth weight live births for black infants.

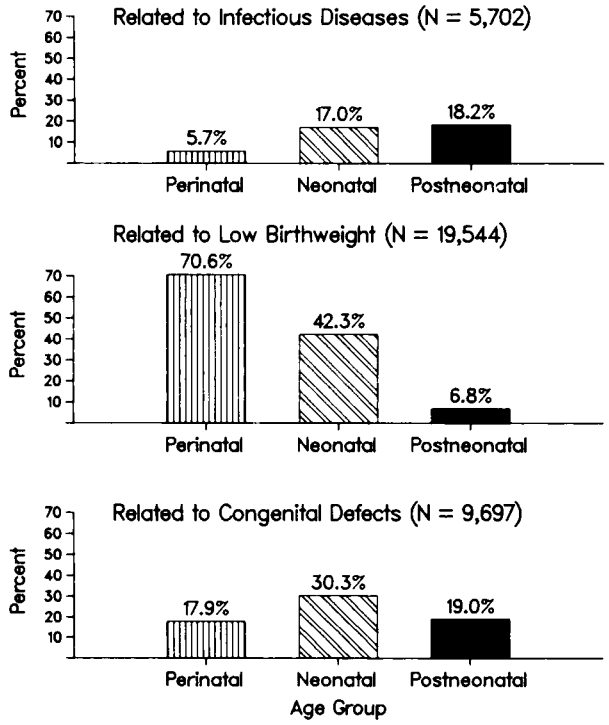

Fig 1. Proportion of infant deaths related to infectious diseases, low birth weight, or congenital defects by age group, United States, 1980.

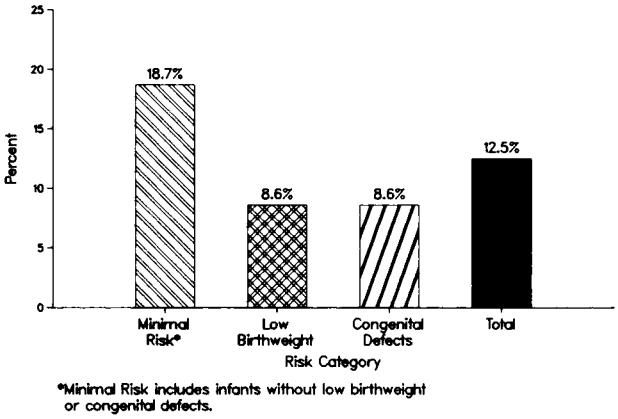

Fig 2. Proportion of infant deaths related to infectious diseases by risk category, United States, 1980.

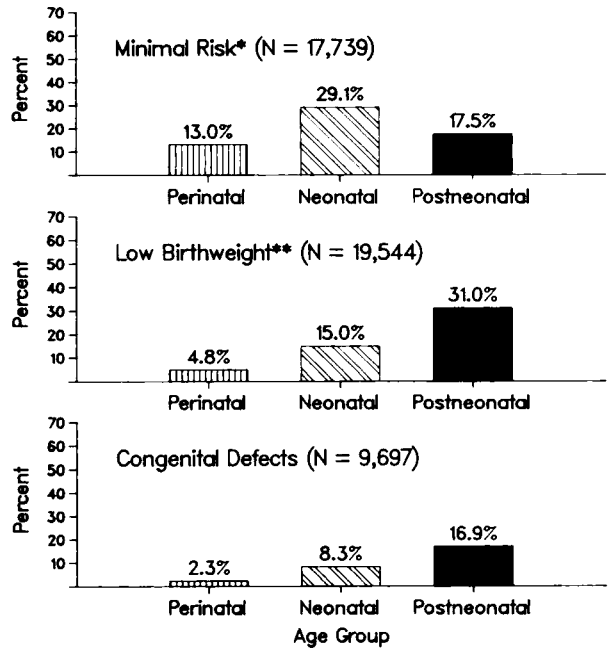

Fig 3. Proportion of infant deaths related to infectious diseases by age group and risk category, United States, 1980.

The proportion of deaths related to infectious diseases did not vary by sex for any age group (boys 12.6%, girls 12.3% overall), although the number of deaths was greater for boys (n = 3,262) than for girls (n = 2,440). When regions were compared, the South had the highest number (n = 2,348), proportion (13.8%), and rate of deaths (1.9/1,000 live births) related to infectious diseases (Table 5).

Perinatal infections, pneumonia, and sepsis accounted for the majority of infectious disease-related deaths (Table 6). Perinatal infections were involved in almost 5% of all infant deaths and represented 39% of the infectious disease-related deaths. Pneumonias were related to nearly 4% of all infant deaths. Bacterial sepsis and/or meningitis were related to 3% of all infant deaths and represented 22% of all infectious disease-related deaths.

DISCUSSION

Federal health priorities include 15 areas in which gains could be expected by 1990.[11] One of these goals is to reduce infant mortality by at least 35% by 1990, ie, to fewer than nine deaths per 1,000 live births. Regrettably, the time needed to achieve this goal may be lengthening. The rate of decrease in infant mortality rates decreased to less than that predicted for 1983 to 1984; postneonatal mortality rates are increasing.[5]

Maternal-infant care programs and health education, although worthwhile in other respects, have not yet proven to be a cost-efficient means of decreasing infant mortality and low birth weight on a national level. Recent data suggest that the percentage of low birth weight infants born each year has not changed, although advances in expensive intensive care techniques have led to increased survival of low birth weight infants.[4,9,12] For infants weighing more than 1,000 g at birth, cost-benefit analyses suggest that the financial benefit to society of therapy for newborns outweighs this therapy's cost. This benefit does not, at present, outweigh cost for those of lower birth weights.[26–28] On a broader scale, programs directed toward decreasing maternal smoking and alcohol use cannot be expected to affect the disparity in low birth weight rates between black and white infants.[13]

Congenital defects, like low birth weight, are another important cause of infant mortality. Rates of birth defects-related mortality have not declined in the past decade.[8] Regrettably, the prevention of birth defect-related mortality is not feasible until the pathogeneses of these defects have been determined.[8] Unlike the prevention of low birth weight and congenital defects, the prevention of infectious diseases has proven to be cost-effective on a national level in terms of vaccination,[14–20] sanitation,[29–31] and therapeutic programs.[32,33] Although not specifically studied in children younger than 1 year of age, measles, polio, diphtheria, pertussis, and tetanus vaccines have been cost-effective and have decreased morbidity and mortality. Furthermore, it is widely accepted that the dramatic reduction in infant mortality rates in the first half of this century was due to advances in these areas.[1,4,7,8]

We used national data listing multiple causes of death for a given individual to obtain an estimate of the proportion of infant deaths that were related to infectious diseases but could not assess the relative importance of infectious diseases in a given death. The accuracy of this estimated proportion cannot be fully assessed with the data at hand, but the estimate is likely to underrepresent the contribution of infectious diseases for at least three reasons. First, we did not evaluate the occurrence and effect of maternal infectious diseases that may have led to early delivery, the birth of a low birth weight infant, and/or the birth of an infant with congenital defects. Second, the death certificate for a perinatal death related to intrauterine infection may not include an infectious disease as a cause of death.[10] Third, we did not include many ICD codes that were nonspecific but suggested an infectious process in our "infectious disease-related" category.

These analyses show that in 1980 almost 400,000 years of potential life were lost from infant deaths in which infectious diseases were a listed cause of

TABLE 5. Percentages and Rates of Infant Deaths Related to Infectious Diseases, by Region, United States, 1980

Region	% of Deaths	Rate (per 1,000 live births)
Northeast	12.1	1.48
North central	11.5	1.43
South	13.8	1.90
West	11.7	1.31

TABLE 6. Infectious Diseases Associated With Infant Deaths*

Cause	International Classification of Diseases Codes	No. (%) of Infant Deaths
Perinatal infections	770.0, 771, 777.5	2,199 (38.6)
Pneumonia	480–486	1,743 (30.6)
Bacterial sepsis	036.2, 038	806 (14.1)
Bacterial meningitis	036.0, 320	448 (7.9)
Chorioamnionitis	762.7	240 (4.2)
Intestinal infections	001–009	172 (3.0)
Other infectious diseases	†	960 (16.8)
Total	†	5,702 ‡

* Cause listed as one of as many as 20 causes of death for a given individual. Perinatal infections include congenital pneumonia, necrotizing enterocolitis, and infections specific to the perinatal period.

† Codes listed in Table 1.

‡ Because more than one infectious disease may be listed as a cause of death, percentages exceed 100%.

death. Infectious diseases were related to 12.5% of infant deaths, for a rate of 1.3 deaths per 1,000 live births in the white population and 2.9 deaths per 1,000 live births in the black population. Moreover, a great many of these deaths occurred among otherwise healthy children.

This study is not intended to detract from the importance of maternal education and prenatal care. It is intended to reemphasize the importance of infectious disease research and of applying this research to programs for the prevention of infectious diseases in pregnant women, newborns, and infants. Specific areas include the development, improvement, and application of vaccines for pathogens common in the first year of life (including respiratory syncytial virus, *Haemophilus influenzae*, *Streptococcus pneumoniae*, *Neisseria meningitidis*, rotavirus, and Group b *Streptococcus*). Also of importance is research on the efficacy of maternal immunizations, perinatal antibiotic therapy (eg, for *Chlamydia* and Group b streptococcal infections), and the role of human milk in preventing or modulating infection due to specific pathogens.[17,34,35] A third general area concerns the many high-risk infants who are admitted to neonatal intensive care units each year. It is estimated that a nosocomial infection develops in as many as 25% of these infants and that nearly one-third of nosocomially infected infants die.[36] An increased emphasis on the development of prevention/infection control measures for neonatal intensive care units is warranted, because a substantial reduction in these infections would reduce infant mortality. Finally, the expanding work force includes mothers who must increasingly rely upon day-care centers for their infants' care. The transmission of infectious diseases within these centers may be associated with preventable infant deaths.[37-39]

In conclusion, we suggest that in these times of decreasing federal resources, infectious disease prevention merits intensified attention. Programs should be designed to emphasize proven preventive methods rather than to develop approaches for which efficacy has not been shown in the past.

ACKNOWLEDGMENT

We thank Van P. Munn for technical assistance.

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DR HENRY A. COTTON ON THE NEED TO ENUCLEATE INFECTED TONSILS IN CHILDREN SO AS TO ELIMINATE MENTAL DISORDERS LATER IN LIFE (1922)

One of the most radical somatic therapies in the 1920s was based on Henry Cotton's (1869–1933) "focal infection theory" of mental disorders. According to this theory, toxins produced by bacteria at infection sites in different parts of the body are transported to the brain where they often produce mental disturbances.[1] Henry Cotton, medical director of the New Jersey State Hospital at Trenton, was the chief proponent of the theory that surgical removal of all suspected foci of infection was essential in the treatment of psychotic patients.[2]

He wrote:

> The tonsils are fully as important as the teeth, for among the psychotic group very few if any patients have had their tonsils removed in childhood. Here, again, errors are made in calling tonsils normal when they may be infected. It is easy to diagnose a hypertrophied tonsil, but very frequently a small buried tonsil may be full of pus. It requires a very careful examination before one is qualified to say that the tonsils are normal...*That the children of the present generation are having their infected tonsils enucleated will, we believe, have a definite influence on the elimination of systemic and mental disorders later in life* [Italics mine].

Noted by T.E.C., Jr, MD

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Pediatrics 1987;80;335