ORIGINAL CONTRIBUTION

Trends in Infectious Disease Mortality in the United States During the 20th Century

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Context Recent increases in infectious disease mortality and concern about emerging infections warrant an examination of longer-term trends.

Objective To describe trends in infectious disease mortality in the United States during the 20th century.

Design and Setting Descriptive study of infectious disease mortality in the United States. Deaths due to infectious diseases from 1900 to 1996 were tallied by using mortality tables. Trends in age-specific infectious disease mortality were examined by using age-specific death rates for 9 common infectious causes of death.

Subjects Persons who died in the United States between 1900 and 1996.

Main Outcome Measures Crude and age-adjusted mortality rates.

Results Infectious disease mortality declined during the first 8 decades of the 20th century from 797 deaths per 100 000 in 1900 to 36 deaths per 100 000 in 1980. From 1981 to 1995, the mortality rate increased to a peak of 63 deaths per 100 000 in 1995 and declined to 59 deaths per 100 000 in 1996. The decline was interrupted by a sharp spike in mortality caused by the 1918 influenza epidemic. From 1938 to 1952, the decline was particularly rapid, with mortality decreasing 8.2% per year. Pneumonia and influenza were responsible for the largest number of infectious disease deaths throughout the century. Tuberculosis caused almost as many deaths as pneumonia and influenza early in the century, but tuberculosis mortality dropped off sharply after 1945. Infectious disease mortality increased in the 1980s and early 1990s in persons aged 25 years and older and was mainly due to the emergence of the acquired immunodeficiency syndrome (AIDS) in 25- to 64-year-olds and, to a lesser degree, to increases in pneumonia and influenza deaths among persons aged 65 years and older. There was considerable year-to-year variability in infectious disease mortality, especially for the youngest and oldest age groups.

Conclusions Although most of the 20th century has been marked by declining infectious disease mortality, substantial year-to-year variation as well as recent increases emphasize the dynamic nature of infectious diseases and the need for preparedness to address them.

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OVER THE LAST 100 YEARS, North America and Europe have experienced a substantial decline in mortality and an increase in life expectancy. The "theory of epidemiologic transition" attributes these trends to the transition from an "age of pestilence and famine," in which the mortality pattern was dominated by high rates of infectious disease deaths, especially in the young, to the current "age of degenerative and man-made diseases" in which mortality from chronic diseases predominates.[1,2] According to estimates from the Global Burden of Disease Study, infectious diseases now account for only 4.2% of all disability-adjusted life years lost (DALYs, a measure of the burden of diseases and injuries) in countries like the United States with established market economies, whereas chronic and neoplastic diseases account for 81.0%.[3]

Until recently, it was assumed that the epidemiologic transition had brought about a permanent reduction in infectious disease mortality in the United States. However, the emergence or reemergence in the 1980s of such diseases as the acquired immunodeficiency syndrome (AIDS) and tuberculosis demonstrated that gains against infectious diseases cannot be taken for granted.[4,5] An outbreak of avian influenza in Hong Kong in late 1997 by a strain (H5N1) not previously known to infect humans[6] is a reminder that pandemic influenza continues to pose a threat.

In the United States, mortality due to infectious diseases increased 58% from 1980 to 1992,[7] a trend that was unforeseen. To determine when this trend began and to characterize longer-term trends in the United States, we examined US mortality records since 1900, when the federal government first began to track mortality data annually.

METHODS

Sources of Mortality Data

Data were obtained from yearly tabulations of causes of death on file at the Division of Vital Statistics of the Centers for Disease Control and Prevention's National Center for Health Statistics and from public use mortality data tapes from 1962 through 1996.

The US federal government began publishing mortality statistics on an annual basis in 1900 after establishment of the

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death-registration system.[8] Initially, data were gathered only from the "death-registration area," which included 10 states, the District of Columbia (collectively known as the "death-registration states"), and 153 cities outside these states. The system was gradually expanded to include all states by 1933. All registered deaths were entered into the system for every year except 1972, when a sample of half of all deaths was entered. Deaths occurring in military personnel outside the United States were not included.[8]

The cause or causes of death obtained from death certificates were coded according to the particular revision of the *International Classification of Diseases* (*ICD*) that was in use at the time (successive revisions were implemented starting in 1900 [*ICD-1*], 1910 [*ICD-2*], 1921 [*ICD-3*], 1930 [*ICD-4*], 1939 [*ICD-5*], 1949 [*ICD-6*], 1958 [*ICD-7*], 1968 [*ICD-8*], and 1979 [*ICD-9*]). The underlying cause of death was selected from the array of medical conditions listed on the death certificate according to standardized algorithms.[8] For this study, only the underlying cause of death was considered when multiple causes of death were listed.

Population data used in the calculation of mortality rates were also obtained from the National Center for Health Statistics. The data for years prior to 1933 included only the population of the death-registration states or death-registration area, corresponding to the scope of the mortality data being used.

Overall Infectious Disease Mortality

From 1900 through 1948, tables for the death-registration area showing mortality by each cause were analyzed. From 1949 through 1996, tables with mortality broken down by 252 to 282 causes were examined. Deaths due to diseases or categories of diseases that are always or almost always infectious were summed for each year to give the total number of infectious disease deaths. These diseases (using the original terminology) were typhoid fever, typhus fever, relapsing fever, malaria, smallpox, measles, scarlet fever, pertussis, diphtheria, croup, influenza, miliary fever, asiatic cholera, cholera nostras, dysentery, plague, yellow fever, leprosy, erysipelas, purulent infection, septicemia, glanders, anthrax, rabies, tetanus, mycoses, tuberculosis, rickets, syphilis, gonococcus infection, other "epidemic, endemic, or infectious diseases," acute articular rheumatism (1900 through 1920), acute rheumatic fever (1921 and later), encephalitis, meningitis, acute poliomyelitis, otitis media, mastoiditis, acute endocarditis, chronic or unspecified endocarditis (1930 to 1940, 1949 and later), "chronic affections of the [heart] valves and endocardium" (1941 to 1948), acute bronchitis, bronchopneumonia, pneumonia, pleurisy, lung abscess, gangrene of the lung, diarrhea, enteritis, ankylostomiasis, intestinal parasites, appendicitis, infections of the kidney, typhlitis, hydatid tumor of the liver, abortion with septic conditions, ectopic gestation with septic conditions, puerperal septicemia, infections of the newborn, gangrene of the skin, furuncle, acute abscess, osteomyelitis, cellular immune deficiency (1980 through 1986), and AIDS (1987 and later).

Disease Categories

Nine categories of infectious disease were analyzed as separate categories: pneumonia and influenza (analyzed as a single category), tuberculosis, diphtheria, pertussis, measles, typhoid fever, dysentery, syphilis ("syphilis and its sequelae"), and AIDS. These categories were also analyzed as a 9-cause aggregate. The first 8 were chosen because they were the most common infectious causes of death in the first half of the century.[9,10] Tabulations, by age, of mortality rates in the death-registration states were available for each of these diseases for the entire study period One additional cause of death, acute poliomyelitis, was also examined. Since data were not available for all years and age-specific rate tables have not been compiled, poliomyelitis mortality was not included in the 9-cause aggregate.

Data on AIDS deaths were obtained from public use data files from 1980 to 1996 by counting all deaths in which the underlying cause was coded as 042.0 to 044.9 (AIDS-related codes, first used in 1987) or 279.1 ("cellular immune deficiency," the code under which AIDS was placed prior to 1987).[7,11]

Age Categories and Age Adjustments

To examine age-specific trends, we analyzed the 9-cause aggregate, which included the majority of infectious disease deaths. The 11 age categories from the original tabulations were merged to form 5 mutually exclusive age groups (0-4 years, 5-24 years, 25-44 years, 45-64 years, and ≥65 years). Where indicated, mortality rates were age-adjusted to the projected year 2000 population by the direct method[12] using the original 11 age categories.

Adjustments for *ICD* Revisions

To adjust for revisions in the *ICD*, comparability ratios were applied to the data.[9,13] These comparability ratios were determined by coding deaths at the years of *ICD* changes using both the old and the new classification and then comparing the results. Comparability ratios were not available to adjust for the changes between *ICD-1* through *ICD-4*. All comparability ratios since the change to *ICD-4* were available for pneumonia and influenza, tuberculosis, and syphilis. No ratios were needed for AIDS, which was not diagnosed before the implementation of *ICD-9*. For the other 5 disease categories, 17 of the 25 comparability ratios were available for the changes that took place after *ICD-4*.

Analysis of Trends

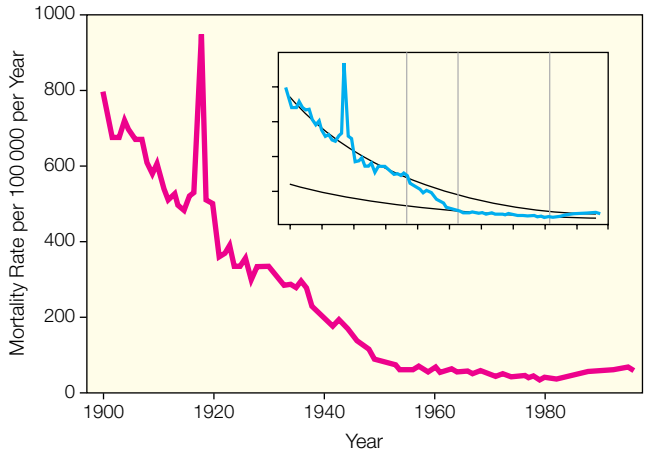
Linear regression was used to estimate the magnitude of trends in mortality rates. In each case, the model included the logarithm of the mortality rate as the dependent variable and the year as the independent variable. Mortality rates from 1918 through 1922 were removed from the data so that trends could be calculated without being influenced by the 1918 influenza pandemic.

RESULTS

Overall Trends

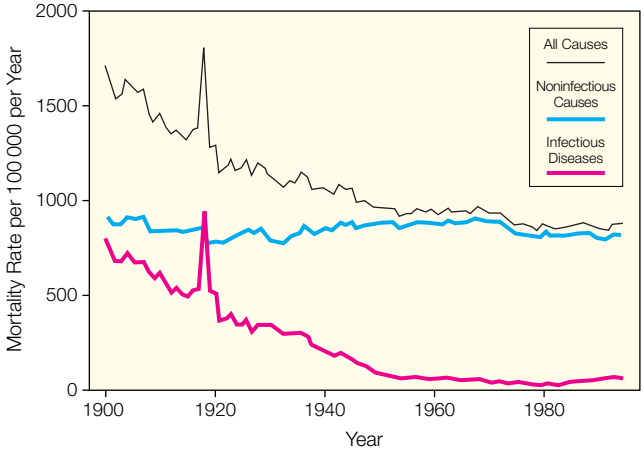
Infectious disease mortality in the United States during the 20th century has been characterized by 4 trends as well as a pro-

Figure 1. Crude Infectious Disease Mortality Rate in the United States From 1900 Through 1996



The inset shows the same mortality curve (blue line) with the fitted regression lines for 2 (1900-1937 and 1953-1980) of 4 segments. The boundaries between the segments are indicated by the vertical dotted lines.

Figure 2. Crude Mortality Rates for All Causes, Noninfectious Causes, and Infectious Diseases



nounced spike attributable to the 1918 influenza pandemic (FIGURE 1). From 1900 to 1937, the crude infectious disease mortality rate decreased by approximately 2.8% per year from 797 deaths per 100 000 persons in 1900 to 283 in 1937. This was followed by a 15-year period during which the rate fell by 8.2% per year to 75 deaths per 100 000 in 1952. The decline then slowed again to 2.3% per year until 1980 (36 deaths per 100 000) after which mortality increased by 4.8% per year to 63 deaths per 100 000 in 1995. In 1996, infectious disease deaths decreased for the first time since 1982, falling to a rate of 59 deaths per 100 000.

The decline in infectious disease mortality paralleled the drop in all-cause mortality during the first half of the 20th century (FIGURE 2). The crude mortality rate from noninfectious causes remained relatively constant during this period, although there was some year-to-year fluctuation. Increases generally occurred in the same years that increases were registered in the infectious disease mortality rate.

Trends in the 9-cause aggregate of infectious disease mortality were similar to trends in overall infectious disease mortality for the 4 time periods (rates of change: –2.7%, –7.8%, –2.3%, and +6.1% per year for earliest to latest time periods). The shape of this curve changed little when the data were age-adjusted to the projected year 2000 population (rates of change: –2.1%, –8.0%, –2.4%, and +4.6% per year), although the decrease in the first segment and increase in the last segment were less prominent. Adjustment of the data to account for changes in disease classification also resulted in little change in the general shape of the curve (rates of change: –2.8%, –7.0%, –1.8%, and +6.1% per year).

Trends by Age Group

The 9-cause aggregate used to examine age-specific trends included 62% to 78% of all infectious disease deaths in all years except 1918, when it included 87%. There was no significant trend in this ratio over the course of the study ($P>.05$).

Trends in the 9-cause aggregate varied by age group (FIGURE 3). The decline in the mortality rate in the first 8 decades of the century was seen in all age groups. The increase after 1981 was seen only in persons aged 25 years and older. In the 25- to 44-year-olds and 45- to 64-year-olds, the increase after 1981 was primarily due to deaths from AIDS, while in the oldest age group (≥65 years), the increase was primarily due to increased deaths from pneumonia and influenza.

During the first decade of the century, the 9-cause aggregate caused a substantial proportion of all deaths in 5- to 24-year-olds (average: 48% of all deaths) and 25- to 44-year-olds (43%). Tuberculosis alone accounted for more than 25% of deaths in both age groups. By the 1970s, infectious diseases caused only 3% of deaths in these age groups.

The 1918 spike in mortality was very pronounced in the 5- to 24-year-olds and the 25- to 44-year-olds (respective peaks: 3.6 and 4.0 times the rates predicted by regression). The mortality rate in that year was of even greater magnitude in the youngest age group, although the spike was not as large relative to the rates immediately before and after. The spike was less prominent in the 45- to 64-year-olds and was hardly discernible in the oldest age group. Much smaller increases in infectious disease mortality occurred in the youngest age groups during the influenza pandemics of 1957 (the "Asian flu") and 1968 (the "Hong Kong flu").

The year-to-year fluctuation in mortality also varied by age group. This fluctuation was most pronounced in the youngest and oldest age groups, reflecting the large contribution of influenza and pneumonia to mortality in these age groups.

Trends by Disease Category

The proportion of all infectious disease deaths caused by influenza, pneumonia, and tuberculosis averaged 60.1% (FIGURE 4, A). Influenza and pneumonia constituted the largest single disease category, averaging 44.4% of all infectious disease deaths (range: 23.4% in 1906 to 67.2% in 1980). Mortality from tuberculosis was similar to that of pneumonia and influenza during the first half of the century but fell more rapidly than the latter after 1950. Mortality from pneumonia and influenza was highly variable from year to year, while mortality from tuberculosis showed little such variability.

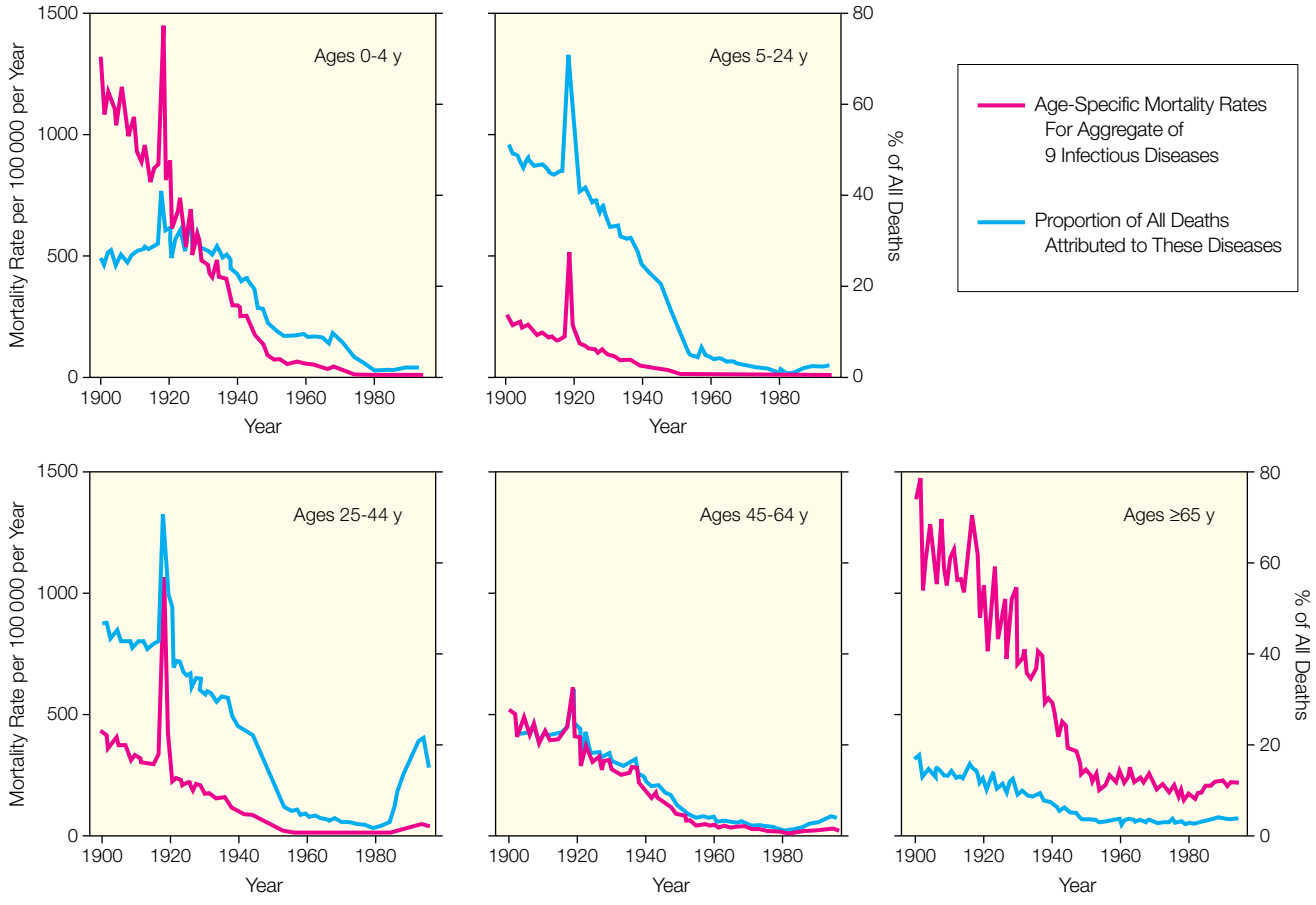
Deaths due to typhoid fever and, to a lesser degree, dysentery, dropped markedly during the first half of the century; by 1950, mortality from these 2 diseases was less than 1 death per 100 000 persons per year (Figure 4, B). Deaths due to diphtheria, pertussis, and measles showed similar trends: there were large decreases during the first half of the century to low levels by 1950 (Figure 4, C). In contrast, polio mortality fell only marginally during the first 4 decades and then increased until the first polio vaccine was licensed in 1955. Polio mortality showed much year-to-year variability as well as a spike in 1916, corresponding to a major epidemic that started in New York City and swept through the northeastern United States during the summer of that year.[14]

Syphilis mortality increased early in the century and remained relatively level until 1940 (Figure 4, D). Between 1940 and 1950, syphilis mortality dropped sharply and was less than 0.2 per 100 000 per year by 1975. AIDS mortality increased throughout the 1980s and early 1990s. By the mid 1990s, the mortality rate was comparable to that of syphilis earlier in the century. From 1995 to 1996, the AIDS mortality decreased for the first time, falling from 16.4 to 11.8 per 100 000.

COMMENT

During the first 8 decades of the 20th century, the infectious disease mortality rate in the United States declined substantially, consistent with the concept of epidemiologic transition. Improvements in living conditions, sanitation, and medical care probably accounted for this trend. But over a 15-year period starting in 1981, this trend reversed, with infectious disease deaths consistently increasing from year to year for the first time since the federal government began tracking mortality statistics. Now, as the end of the century nears, infectious

Figure 3. Age-Specific Mortality Rates for an Aggregate of 9 Infectious Diseases and Proportion of All Deaths Attributable to These Diseases

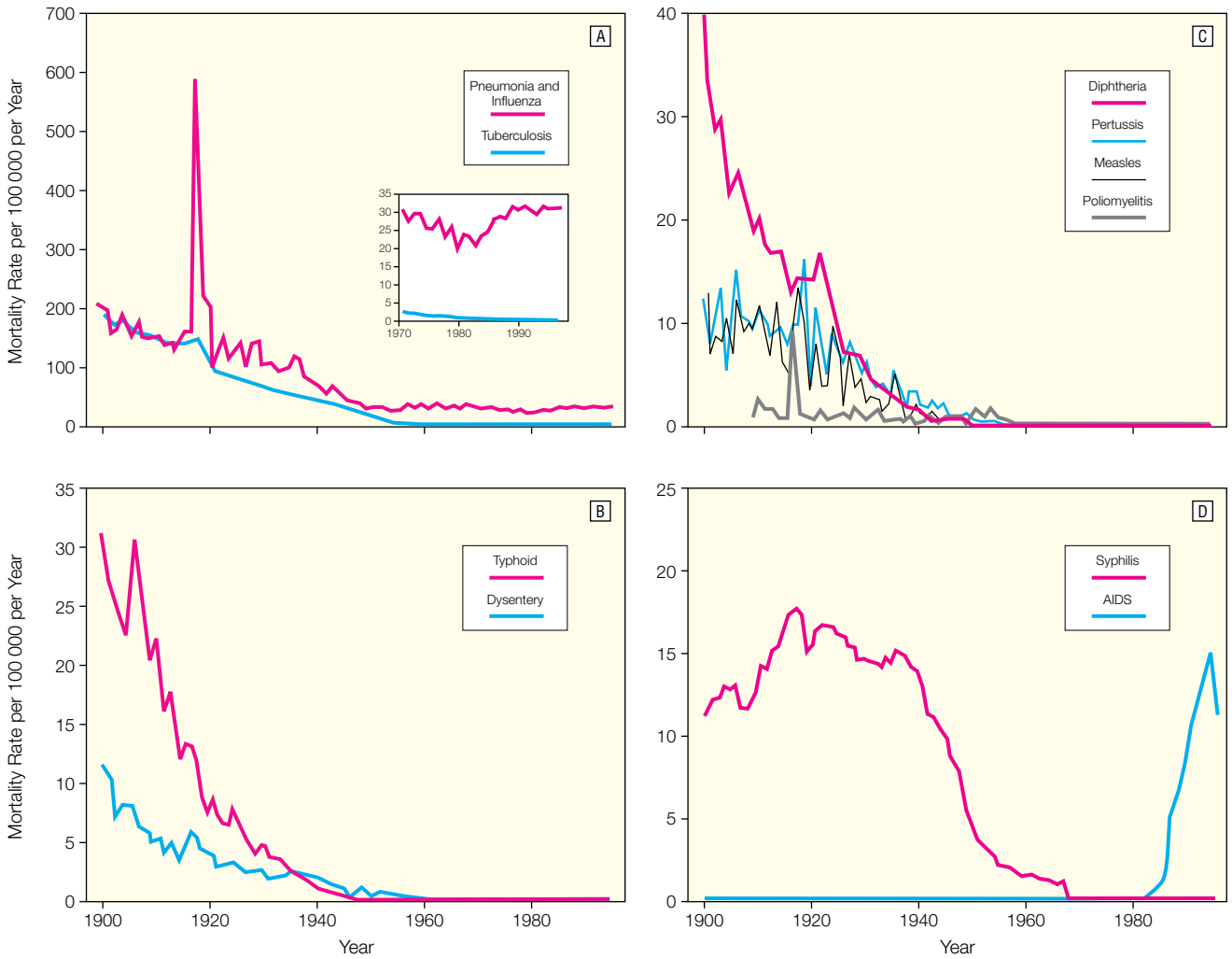


disease deaths may again be declining; a 7% drop was registered in 1996, largely because of a substantial decline in AIDS mortality.[15,16]

A closer examination of the decline from 1900 to 1980 revealed that it was characterized by 3 distinct periods. During the first (1900 to 1937) and third (1953 to 1980) periods, infectious disease mortality fell by 2.3% to 2.8% per year. During the 15 years between these periods, the annual decline in the infectious disease mortality rate accelerated to 8.2%. The disease categories that contributed most to this decline were pneumonia and influenza, which fell sharply from 1938 to 1950 and subsequently leveled off for several years, and tuberculosis, which fell abruptly from 1945 to 1954 and continued to fall until the mid 1980s. These declines coincided with the first clinical use of sulfonamides (1935), antibiotics (penicillin in 1941 and streptomycin in 1943), and antimycobacterials (streptomycin, first used against tuberculosis in 1944, para-aminosalicylic acid in 1944, and isoniazid in 1952).[17] However, the reasons for the steep decline from 1938 to 1952 are probably many and cannot be determined by examination of the mortality data alone.

The use of mortality data to evaluate disease burden has limitations. For one, the mortality rate is an incomplete indicator of disease burden in that it does not account for varying numbers of potential years of life lost at different ages or for productive years lost because of disability. Indicators such as the DALY, used as the principal metric in the Global Burden of Disease project, would provide a different perspective on the overall burden of disease.[3] Such indicators have limitations as well, most notably that they depend on the particular system used to

Figure 4. Crude Mortality Rates for 10 Infectious Diseases



The inset in Figure 4A shows the pneumonia and influenza mortality rate from 1970 to 1996. Statistics for poliomyelitis were not listed separately on mortality charts until 1909 (Figure 4C). AIDS indicates acquired immunodeficiency syndrome.

weight deaths and disability.[18,19]

Furthermore, mortality statistics are only as accurate as the data provided by physicians who fill out death certificates. Validation studies have shown that the major *ICD* disease category (ie, categories such as infectious diseases, respiratory diseases, or cardiovascular diseases) listed as the underlying cause of death on death certificates differs from that determined by autopsy in 12% to 29% of cases.[20-23] This may lead infectious diseases to be imprecisely represented in mortality data.[24,25] In addition, changes over time in autopsy rates and in diagnostic capabilities may affect trends in mortality statistics. Despite these deficiencies, no other surveillance data can match the completeness and longevity of mortality data.

The decrease in mortality before 1980 and the increase after 1981 are not likely to be due to changes in the age structure of the US population alone. These trends remain when the data are age-adjusted and adjusted for changes in *ICD* coding. The latter adjustment should be considered an approximation, since each of the comparability factors used in this adjustment had been derived from mortality data from a single year and may not be applicable to other years.

The volatile nature of infectious diseases is apparent in Figure 1. The sawtooth appearance of the first half of the curve reflects the periodic spikes in incidence that characterize the epidemiology of diseases such as measles (every 2-5 years),[26] pertussis (every 2-5 years),[27] diphtheria (approximately every 10 years),[28] and especially influenza (every 2-3 years).[29] Infectious diseases of a more chronic nature, such as tuberculosis or AIDS, show much less year-to-year variability.

The jump in mortality during the 1918 influenza pandemic, in which 20 to 25 million persons worldwide died from "Spanish flu," is the most visible manifestation of the potential volatility of infectious diseases. The spike in mortality was most prominent in 5- to 44-year-olds, reflecting the disproportionate mortality suffered by young adults during that pandemic.[30] Although influenza pandemics since 1918 have not caused mortality on the same scale, it is conceivable that a future pandemic with a particularly virulent strain could cause another large spike in the infectious disease mortality curve.

Even as the 20th century closes with much reduced death rates from infectious diseases, numerous episodes as well as recent trends remind us how dynamic the factors are that influence the emergence and reemergence of infectious diseases.[4] Infectious disease mortality did not continue to decline as one might have predicted had Figure 1 been constructed in 1980. And since there is no guarantee that future trends will be stable, it remains important to be vigilant over the threats posed by microbes.[31]

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