MEASLES MORTALITY: A RETROSPECTIVE LOOK AT THE VACCINE ERA[1]

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Barkin, R. M. (Bureau of Epidemiology, CDC, Atlanta, GA 30333). Measles mortality: A retrospective look at the vaccine era. *Am J Epidemiol* 102:341–349, 1975.

Measles mortality provides an indicator in defining the population at greatest risk of experiencing serious complications from measles as well as serving as a parameter in assessing the impact of immunization programs. Efforts to vaccinate susceptible children have helped to reduce measles morbidity and mortality in the United States. Mortality rates were highest in children 6–11 months of age. Higher mortality rates were noted in places with less than 10,000 people and in counties having a large percentage of the population with incomes below poverty level. Vaccine should be accessible to all populations, but intensive efforts need to be directed toward groups at high risk of dying from measles who are suffering from a myriad of other health, social, and economic problems.

Measles; mortality; vaccination

More than a decade has passed since live-virus measles vaccine was licensed for use in the United States. Vaccine licensure in 1963 followed the isolation of wild measles virus by Enders and Peebles in 1954 (1) and its subsequent cultivation and attenuation on chick embryo cells by Milovanovic and co-workers (2, 3). The vaccine has continued to be effective and safe.

Local, state, and national health programs have distributed nearly 70 million doses of live-virus vaccine, nearly 25 per cent of which were federally funded. Eradication programs first received federal sup-

port in 1965, and they helped produce the striking reduction in the number of cases of measles noted in the United States. However, in 1969, federal priorities shifted to an intensive rubella vaccination program and a resurgence of measles took place. This upward trend in reported morbidity and mortality from measles was finally reversed in late 1971 when federal funds were reinstated, and nearly 8 million doses of vaccine were distributed annually (4). The widespread use of measles vaccines accounts for the dramatic decline in measles-associated morbidity and mortality in the United States during the last decade (figure 1).

As we move into the second decade of vaccine availability, evaluation of the continuing impact of measles vaccination is required. Reports describing the status of measles control in the United States have dealt primarily with the epidemiology of measles and emphasized morbidity, immunity levels (by immunization and/or natural disease), and vaccine usage as indicators of past successes and potential progress (4–8). In contrast, this paper will

focus on deaths caused by measles and thereby provide another measure of the impact of measles vaccines in the United States.

METHODS

Line listings of recorded measles deaths in the United States compiled by the National Center for Health Statistics (NCHS) provided age, sex, race, state and county of residence, and month of death data on all persons with death attributed to measles. The six-year period 1958–1963 was selected to provide data on measles mortality prior to vaccine licensure, while 1965–1967 and 1968–1970 were analyzed separately and together to evaluate the impact of vaccine on mortality; 1970 is the latest year for which detailed mortality data are currently available.

Income-specific mortality rates were calculated by stratifying the county of residence of individuals who died of measles in 1962–1969 according to the percentage of individuals with incomes below poverty level (1960 Office of Economic Opportunity standards[3]) and determining the number of deaths and population of these counties. The unavailability of data necessitated different year groupings for income-specific mortality rates. The death-to-case ratio was computed by dividing age-specific mortality by age-specific morbidity data.

Morbidity data were derived from two sources. The Center for Disease Control compiles weekly morbidity information on reported measles cases in the United States through the cooperation of state and local health departments (4). A second major source of morbidity data is the estimated number of measles cases compiled annu-

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[3] Defined by Social Security Administration guidelines using nutritionally adequate food as the basis for determination of poverty income cutoffs. In 1960, 22.2 per cent of the population was at poverty level income or below. For a family of four, this level was $3017 ("Revision in Poverty Statistics, 1959 to 1968," Current Population Reports, Series P-23, No. 28, August 12, 1969. Bureau of the Census, US Department of Commerce).

ally by the National Center for Health Statistics from a health interview survey conducted in cooperation with the Bureau of the Census (9). The age distribution of measles patients was available from data collected by the Center for Disease Control (4, 5).

Rates for the periods 1958–1963 and 1960–1963 were based on the 1960 Census. Estimates of 1966, 1969, and 1967 population were derived from interpolations of 1960 and 1970 Census information and used as the base for 1965–1967, 1968–1970, and 1965–1970, respectively. However, 1960 Census data were used in the calculation of income-specific mortality rates for the entire period analyzed.

RESULTS

Average annual measles mortality rates have slowly declined since the early 1900's from an average of 10 deaths from measles per 100,000 population early in the century to 0.23 per 100,000 during the six-year period 1958–1963, when 2523 deaths from measles were recorded. Following vaccine licensure, the average annual mortality rate dropped to 0.065 deaths per 100,000 population in 1965–1970. A relatively smaller decline in rates was noted in the three-year period 1965–1967, while the most substantial decrease in mortality rates was observed in 1968–1970. The total number of deaths more than quartered in 1965–1970, with 618 deaths recorded, only 154 of which occurred in 1968–1970. Reported measles cases remained relatively constant before the introduction of vaccine in 1963, and it was not until 1965 that the first marked decrease in incidence was noted (figure 1).

Seasonal trends. Deaths attributed to measles occurred primarily in the late winter and the spring, corresponding to the seasonal pattern of measles cases in the United States. The largest number of cases reported and deaths recorded before and after vaccine licensure was in April.

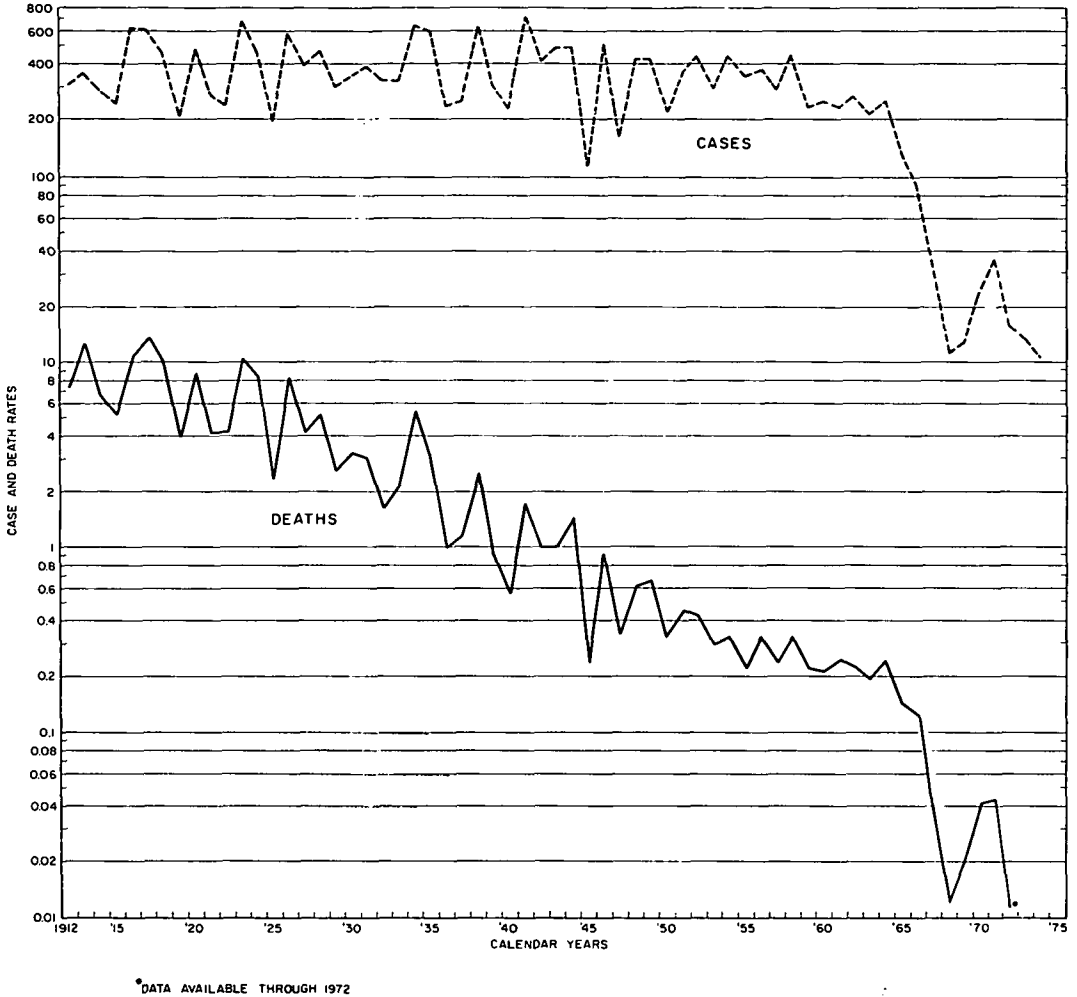*Geographic distribution.* Measles mor-

FIGURE 1. Reported measles cases and deaths per 100,000 population, United States, 1912–1974.

tality rates by state were consistently higher in the southern part of the United States. Although statewide mortality rates were lower after vaccine licensure, the geographic clustering of states in the higher quartiles was similar to that noted prior to vaccine licensure (figure 2). In 1968–1970, Arizona, Mississippi, Montana, and New Mexico had the highest mortality rates. The same geographic distribution of states in the south with high mortality rates was noted for race-specific mortality rates.

Population size of place of residence. The population size of the place of residence was found to have a large effect on measles mortality rates. Mortality rates in places with 10,000 or more people were lower than rates in places with less than 10,000 residents. Following vaccine licensure, the relative percentage decreases in population-specific mortality rates were greatest in places with populations under 10,000. The differential mortality rates in larger and smaller communities declined with increasing vaccine usage (table 1).

Income level. Income-specific mortality rates increased as the percentage of residents with incomes below poverty level increased. Counties with over 60 per cent of the population with incomes below poverty

A. 1958-1963

DEATHS PER 100,000
POPULATION

☐ 0.0-0.154
☐ 0.155-0.226
▨ 0.227-0.339
▨ ≥0.340

B. 1968-1970

DEATHS PER 100,000
POPULATION
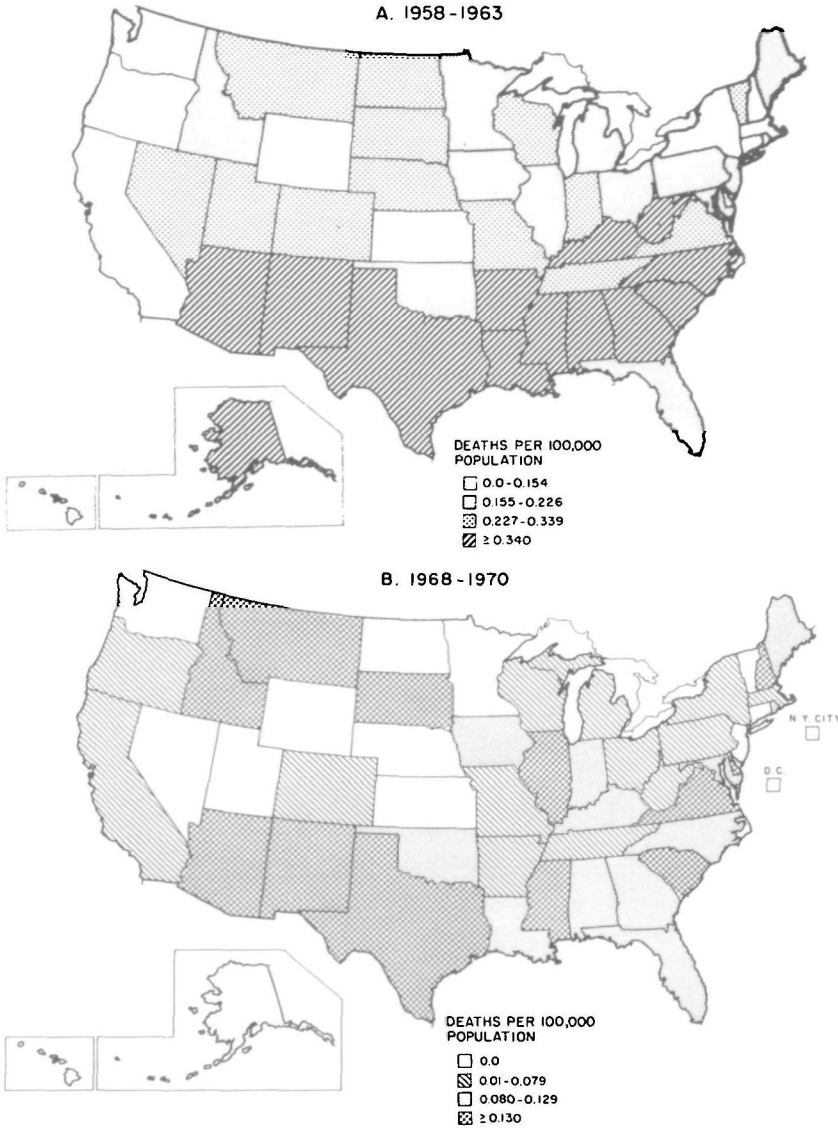
☐ 0.0
▨ 0.01-0.079
☐ 0.080-0.129
▨ ≥0.130

FIGURE 2. Average annual measles mortality rates, United States, 1958-1970.

level had the largest percentage diminution in mortality rates, dropping from 0.92 average annual deaths per 100,000 population in 1962-1963 to 0.09 deaths per 100,000 in 1967-1969 (table 2).

Age and sex. Age-specific mortality rates decreased with increasing age, the rate being lowest for those 15 years of age or over (table 3 and figure 3A). Mortality rates for infants increased substantially at six months of age and were greatest for those six to 11 months of age. Of children who died when one to four years of age, the age-specific mortality rate was highest for one-year-olds and decreased with age (table 3). The percentile distribution in each age group of population of the place of residence was similar.

Following the licensure of measles vaccines, age-specific mortality rates decreased in all age groups. The largest decline was noted in 1968-1970. Those

TABLE 1

Average annual measles mortality rate per 100,000 population and (average annual deaths), by year and population size of place of residence, United States, 1960–1970

Population size of place of residence	1960–1963	1965–1967	1968–1970
≥1.0 million	.13 (23.5)	.07 (12.7)	.03 (6.0)
100,000–999,999	.16 (55.0)	.09 (31.3)	.02 (8.0)
10,000–99,999	.17 (78.5)	.07 (35.0)	.02 (10.0)
<10,000	.29 (140.0)	.15 (127.0)	.03 (27.3)
Total	.22 (297.0)	.11 (206.0)	0.3 (51.3)

TABLE 2

Average annual measles mortality rate per 100,000 population and (average annual deaths), by year and income level, United States, 1962–1969

% population in county with income below poverty level*	1962–1963		1964–1966		1967–1969	
	White	Black/other	White	Black/other	White	Black/other
≤19.9	.13 (147.5)	.03 (0.1)	.10 (114.3)	.03 (1.0)	.02 (17.1)	.00 (0.0)
20.0–39.9	.25 (92.4)	.13 (8.1)	.22 (80.5)	.16 (10.3)	.03 (12.2)	.05 (3.2)
40.0–59.9	.33 (23.6)	.49 (23.8)	.40 (29.1)	.32 (15.6)	.08 (5.7)	.05 (2.5)
≥60.0	.87 (10.5)	.97 (79.9)	.75 (9.0)	.72 (59.4)	.07 (0.8)	.09 (7.6)
Total	.18 (274.0)	.56 (111.9)	.16 (232.9)	.43 (86.3)	.02 (35.8)	.07 (13.3)

* 1960 Office of Economic Opportunity standards.

under one year of age and over 15 years experienced the smallest decrease in rates. The mortality rate in 1968–1970 was 0.35 deaths per 100,000 in children under one year of age, more than twice that of children one to four years of age (0.15 deaths per 100,000) (figure 3A).

No differences were noted before or after vaccine licensure in sex-specific mortality rates.

Race. In 1958–1970, race-specific mortality rates for the white population remained lower than for the black/other population despite the introduction of measles vaccine in 1963. Reductions in mortality rates were noted for both groups after vaccine licensure, the rate for white populations remaining at less than half of the 0.05 deaths per 100,000 population recorded for black/other populations in 1968–1970.

The largest differences in age-race-specific mortality rates between the white and black/other populations were noted for children four years of age and younger and decreased with increasing age. In children under one year of age the disparity was most striking, the rate in 1968–1970 for white children being one-fourth the rate of 0.95 deaths per 100,000 population for black/other children under one year (table 3).

Income-race-specific mortality rates demonstrated no significant differences in mortality rates between the white and black/other populations in lower income strata. In communities having 60 per cent or more of the population with incomes below poverty level, the white and black/other populations had similar mortality rates. Although decreases after vaccine licensure were noted in all groups, no consistent pattern was noted (table 2).

Death-to-case ratio. The death-to-case ratio provides an excellent basis for assess-

TABLE 3

Average annual measles mortality rate per 100,000 population and (average annual deaths), by year, age and race, United States, 1958–1970

Age (years)	1958–1963				1965–1967				1968–1970			
	White		Black/other		White		Black/other		White		Black/other	
<1	1.62	(56.5)	5.10	(31.3)	.97	(30.4)	2.72	(15.7)	.23	(7.0)	.95	(5.3)
0–5 months	.73	(12.7)	2.46	(7.5)	.49	(7.7)	2.05	(6.0)	.09	(1.3)	.00	(0.0)
6–11 months	2.49	(43.8)	7.70	(23.8)	1.46	(22.7)	3.39	(9.7)	.38	(5.7)	1.95	(5.3)
1–4	1.08	(149.7)	2.55	(59.8)	.51	(64.0)	1.56	(35.3)	.13	(14.7)	.27	(6.0)
1	1.82	(63.7)	5.58	(33.6)	.81	(25.7)	3.48	(19.6)	.24	(7.0)	.94	(5.0)
2	1.03	(36.0)	2.06	(12.2)	.55	(17.0)	1.25	(7.0)	.11	(3.0)	.13	(0.7)
3	.73	(25.0)	1.34	(7.8)	.35	(11.0)	.82	(4.7)	.07	(2.0)	.06	(0.3)
4	.74	(25.0)	1.08	(6.2)	.32	(10.3)	.69	(4.0)	.09	(2.7)	.00	(0.0)
5–9	.43	(69.7)	.41	(10.8)	.20	(33.3)	.30	(8.7)	.05	(9.0)	.04	(1.3)
10–14	.09	(13.2)	.11	(2.3)	.05	(7.7)	.05	(1.3)	.01	(2.0)	.00	(0.0)
15+	.02	(22.3)	.02	(2.5)	.01	(9.3)	.02	(0.3)	.004	(5.3)	.001	(0.7)
Total	.20	(311.4)	.52	(106.7)	.08	(144.7)	.26	(61.3)	.02	(38.0)	.05	(13.3)

ing the severity of disease as reflected by death in different age and population groups. Employing reported measles cases compiled by the Center for Disease Control, and deaths, the death-to-case ratio over the 12-year study period was 9.35 deaths per 10,000 reported cases. Similar computations utilizing National Center for Health Statistics disease estimates provide a much lower death-to-case ratio of 0.68 deaths per 10,000 estimated measles cases. The large discrepancy was probably a reflection of the inaccuracies of current data collection procedures.

Although age-specific attack rates decreased in all age groups in 1965–1970 when compared with prevaccine levels, the largest decrease in attack rates was in the preschool and elementary school children who were the focus of measles control programs (figure 3B).

Age-specific death-to-case ratios demonstrated similar trends prior to and after the licensure of vaccine. Children under one year of age consistently had high death-to-case ratios, with a marked reduction in deaths per 10,000 cases with increasing age. The death-to-case ratio for persons 15 years and older was nearly as high as for infants until 1967 and higher in 1968–1970 (figure 3C).

To determine the true death-to-case ratio, both morbidity and mortality components must be analyzed. Current evidence indicates that cases reported to the Center for Disease Control represent 6–8 per cent of the number of cases actually occurring (4). The estimated cases compiled by the National Center for Health Statistics represent an overestimate of true cases, since only 4–5 million cases could have occurred per year prior to the vaccine era, if better than 95 per cent of the adult population were protected as has been documented by numerous epidemiologic and serologic studies (10). In 1958–1963, the National Center for Health Statistics estimated that 6.5 million cases occurred annually. A part of the overestimates result from the difficulty in distinguishing between measles and other rash diseases by household interview techniques. Indeed, the estimates of the National Center for Health Statistics have a relatively large sampling error. (For example, in 1966 the 95 per cent confidence limit based upon the sample estimate of 2,927,000 cases was 2,003,000 to 3,911,000 cases.)

In addition, fewer than the true number of deaths attributable to measles are recorded as such. Measles may have only been considered to have contributed to

death and the death not be directly attrib-
uted to measles in the line listings of
recorded deaths.

Considering 1) that cases reported to the
Center for Disease Control represent fewer
than 10 per cent of actual clinical cases, 2)
that the National Center for Health Statis-
tics morbidity data overestimate true mor-
bidity, and 3) that the recorded deaths do
not reflect the total directly attributable to
measles, the true death-to-case ratio can
be estimated to be approximately 1.0
deaths per 10,000 measles cases.

DISCUSSION

This paper has attempted to define the
population at greatest risk of dying from
measles and assessing the impact of
measles vaccine on these risk factors. The
delineation of risk factors may provide an
indicator of those populations at greatest
risk of experiencing serious complications
from measles.

In assessing the validity of such an
analysis, it is appropriate to recall a state-
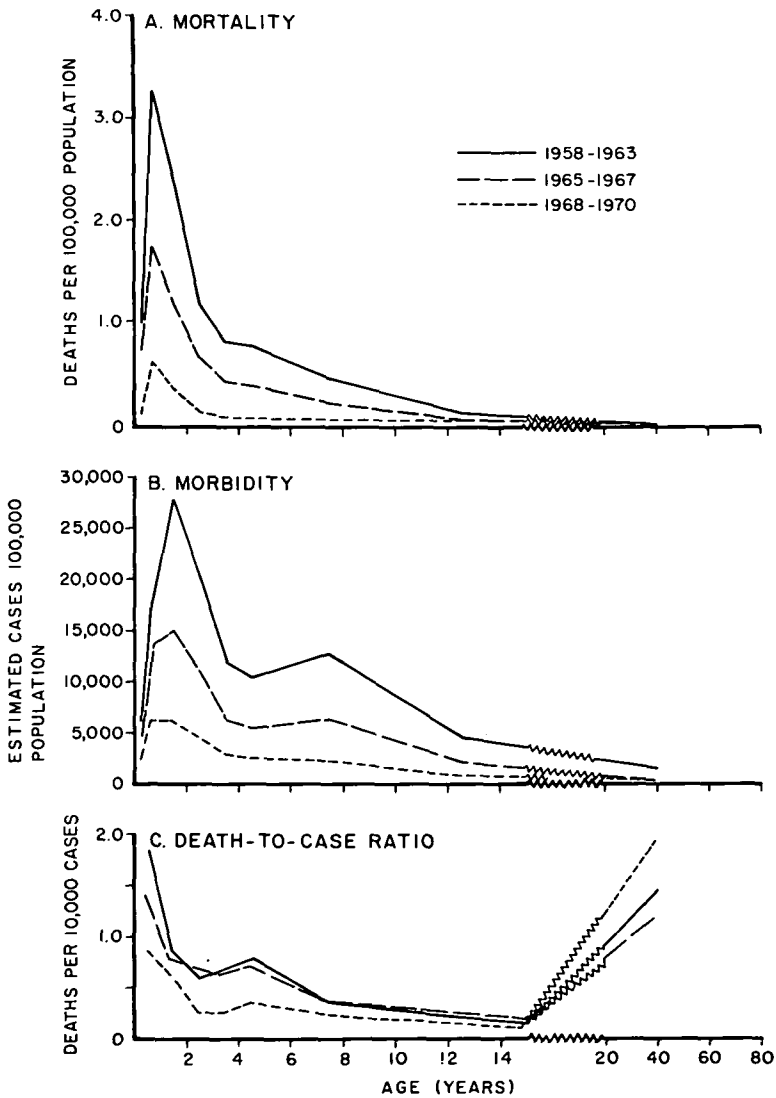ment made in 1933 by A. W. Hedrich:

FIGURE 3. Measles age-specific rates, United States, 1958–1970.

"The research worker in this branch of epidemiology (measles) faces the alternatives of struggling with imperfect raw material or of abandoning his search for information (11)." Data must be interpreted in the context of current local and national priorities, especially when the analysis is retrospective. However, little has changed to make the conclusions less valid and in fact, a resurgence in measles morbidity was noted in 1969–1973.

Since the early 1900's, measles mortality rates have declined subsequent to advances in medical technology and patient management and the introduction of appropriate antibiotic therapy. In the last decade, efforts to vaccinate susceptible children have accounted for recent reductions in measles morbidity and mortality. Quantitatively, the greatest impact was noted in 1968–1970, when reported cases and recorded mortality reached record lows; however, the populations with the highest mortality rates before vaccine licensure continued to have the highest rates after 1963.

Contrary to earlier expectations, measles has not been eradicated (12). Until eradication becomes a reality, programs must be directed at prompt epidemic control combined with vaccination of susceptible populations, particularly those at greatest risk of suffering serious complications.

In focusing attention on children under one year of age, the data serve to define the population at greatest risk of suffering serious measles complications. Respiratory causes of death accounted for nearly 65 per cent of the deaths in this age group (13). The geographic distribution is certainly a reflection of inequities of availability of a host of services, medicine being just one key element. Rural populations residing in counties with a large percentage of the population below poverty levels are reflected in the mortality rates by state (figure 2). The higher mortality rates in some states are not explained simply by a younger population developing measles.

Certainly, the reported experience in other countries has underlined the greater risk to young children and the importance of poor nutritional and health status in contributing to rates of death associated with measles (14–17). Robson and Jones (18) documented that in the United States, measles deaths primarily occur in individuals below established height and weight norms. The 10-State Nutrition Survey conducted in the United States in 1968–1970 indicated that evidence of malnutrition increased as income level decreased and was least common in white persons (19). Death-to-case ratios generally decrease with improving nutrition and health status of a population (20, 21).

These risk factors must be incorporated in ongoing measles control programs. The primary goal of measles vaccination should be the prevention of measles cases, but perhaps even more importantly, a reduction in complications secondary to measles. Certainly, vaccine should be accessible to all populations, but more intensive efforts need to be directed toward high-risk groups who are no doubt suffering from a myriad of social and economic problems and in all likelihood have the least accessibility to adequate health care.

Despite the decreased efficacy of vaccination of children under 12 months of age, mortality data indicate that selective vaccination of six- to nine-month olds must be considered in highly endemic or epidemic areas. Scheduled revaccination at one year of age must be an integral part of any such program (22). Attention must also be focused on the population over 15 who will represent an increasing percentage of measles cases as declining rates of natural infection are observed. The higher death-to-case ratio in this group may be indicative of a greater risk of complications from measles, exposing the unprotected adult to the potential of substantial morbidity.

Important inroads have been made in

reducing measles morbidity and mortality since the licensure of live measles vaccine. As the second decade of vaccine availability evolves, the impact of measles vaccine will require careful assessment. Although mortality can only provide a retrospective analysis, it does serve to define populations in need of attention in establishing future priorities.

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