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THE RESURGENCE OF MEASLES IN THE UNITED STATES, 1989–1990[1]

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ABSTRACT

After almost a decade of relatively few reported cases, a major resurgence of measles occurred in the United States in 1989–1990. The increase primarily involved unvaccinated racial and ethnic minority children less than five years of age residing in inner-city areas. Outbreaks of measles among vaccinated school-aged children continued to occur but had less impact than outbreaks among preschool-aged children. Efforts to prevent measles must be aimed at improving age-specific measles vaccination coverage among preschool-aged children, and implementation of a two-dose measles strategy among school-aged children.

INTRODUCTION

Measles once affected virtually everyone in the United States. Over 500,000 cases were reported annually in the prevaccine era. Since vaccine licensure

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in 1963, measles has become a relatively uncommon disease. Nevertheless, measles outbreaks continue to occur (1, 2), and a resurgence of measles in the United States in 1989 and 1990 has resulted in higher morbidity and mortality from measles than at any time during the past 14 years. This resurgence has been associated with a marked change in the epidemiologic characteristics of measles. Unvaccinated preschool-aged children and persons of racial and ethnic minority groups have been at highest risk.

This review describes the changing epidemiology of measles, explores the reasons for the resurgence, and discusses potential means for better preventing measles in the future.

EPIDEMIOLOGY

Prior to the availability of measles vaccines, approximately 95% of persons living in urban areas of the United States were infected by age 15 years (3). An estimated 4,000,000 to 5,000,000 cases occurred annually, with over 500,000 cases reported each year to public health authorities. With the widespread use of live measles virus vaccines, a major reduction in the reported incidence of measles has been achieved. In 1978, when an intensified effort to eliminate indigenous measles in the United States began (4), a total of 26,871 cases was reported. In 1983, a record low of 1497 measles cases was reported, a reduction of more than 99% compared to the years preceding vaccine licensure. From 1984 through 1988 an annual average of 3700 cases was reported.

Age

In addition to a reduction in total reported cases, a change in the epidemiology of measles occurred after introduction of the vaccine. In the years preceding vaccine licensure, the highest age-specific incidence rates were in children 5 to 9 years old. Since 1980 the highest incidence of measles has been among children under 5 years of age and in persons 15–19 years of age. Incidence rates in 5–9 year olds have been lower than rates in any group except persons 20 years of age or older. The dramatic reduction in disease rates in this age group is largely due to the enforcement of immunization laws that require adequate immunization at entry into school.

In 1989 and 1990 a dramatic increase in cases occurred. In 1989, 18,193 cases were reported (1), and in 1990 a total of 27,786 cases was reported, the largest number since 1977 (2a). The overall incidence of measles increased almost 800% compared to the median incidence in 1980–1988 (Table 1). Measles incidence increased in all age groups, but increased the most in children <1 year and 1–4 years of age. The change in age

Table 1 Incidence[a] of reported measles by age group in the United States, 1980–1988, 1989, and 1990

Age group (years)	1980–1988[b]	1989	1990
<1	5.6	50.5	119.3
1–4	4.7	31.7	59.3
5–9	1.8	9.7	14.9
10–14	3.5	13.1	13.4
15–19	4.5	24.8	17.4
20–24	1.0	8.5	13.3
≥25	0.1	1.0	2.3
Total	1.4	7.3	11.2

[a] Cases per 100,000 population. Rates calculated for all reported cases with known age [18,107 (99.5%) in 1989, 27,678 (99.6%) in 1990], and an extrapolated proportion of cases with unknown age, using census estimates.
[b] Median rate, 1980–1988.

distribution of cases was particularly dramatic. During 1980–1988 a median of 29% of reported cases were <5 years of age (Figure 1). In 1989 the proportion of patients <5 years of age increased to 37%, and in 1990, 48% of patients were in this age group, the first time since national data

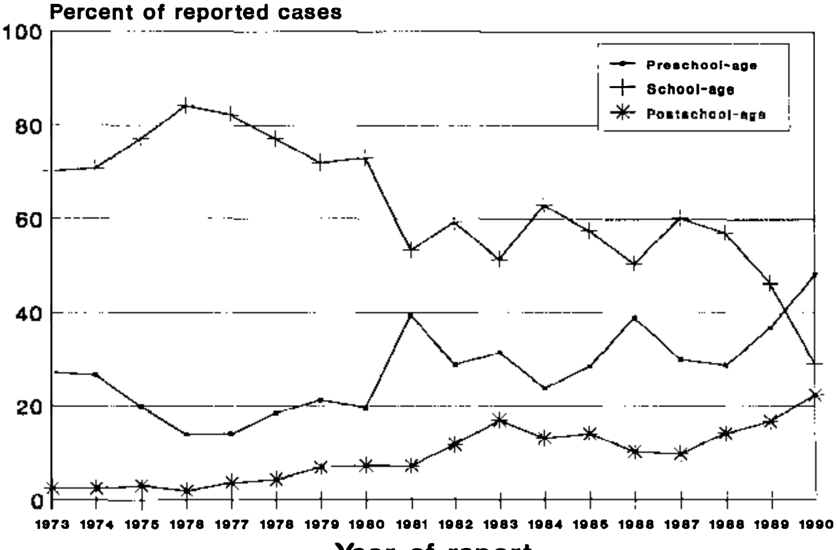

Figure 1 Proportion of reported measles cases by age group in the United States, 1973–1990.

on age became available that the proportion of cases in children < 5 years of age exceeded the proportion of cases in 5–19 year olds. Conversely, the proportion of school-aged persons (5–19 years old) with measles decreased. During 1980–1988, a median of 57% of reported cases were in persons 5–19 years of age, compared with 46% in 1989 and 29% in 1990.

Among preschool-aged children, the age distribution has also changed. From 1980 to 1988, children < 12 months of age accounted for a median of 27% of cases among preschool-aged children, and a median of 8% of all reported cases. In 1990, children < 12 months of age increased to 35% of cases among preschool-aged children, and 17% of all reported cases, the highest proportion of cases in this age group ever reported.

Race and Ethnicity

The increase in measles incidence in 1989 and 1990 was not equally distributed among all racial and ethnic groups. Overall incidence rates in 1989 and 1990[2] were highest for Hispanics (25 and 29 cases per 100,000 population, respectively) and blacks (19 and 12 per 100,000, respectively) and lowest for non-Hispanic whites (5 per 100,000 for both 1989 and 1990). The largest difference in age-specific incidence was among children < 5 years of age. In this age group, the incidence of measles among blacks in 1989 and 1990 was 142 and 87 per 100,000, respectively, and among Hispanics it was 121 and 164 per 100,000, respectively, compared to 16 and 23 per 100,000 among non-Hispanic whites.

Vaccination Status

Vaccination data are available on cases reported since 1985. From 1985 through 1988, 42% of cases occurred in persons who were vaccinated on or after their first birthday (Table 2). During these years, 68% of cases in school-aged children (5–19 years) had been appropriately vaccinated. In contrast, only 16% of cases in children 16 months to 4 years of age were appropriately vaccinated. In 1990, only 19% of reported cases were appropriately vaccinated, the lowest proportion of vaccinated cases since 1985.

In order to understand better the reasons for nonvaccination, unvaccinated persons are classified as (*a*) "vaccine indicated" (unvaccinated persons who should have been vaccinated based on current recommendations); (*b*) "not routinely indicated" (persons with medical contraindications to vaccination, or younger or older than the routine age of vaccination); or (*c*) "other" (groups in which vaccination is difficult to

[2] Race and ethnicity data were not available prior to 1989; data were available for 43% of the cases reported to the Centers for Disease Control in 1989 and 44% of the cases in 1990.

Table 2 Vaccination status (in percentage) of reported measles in the United States, 1985–1988, 1989, and 1990

Classification	1985–1988	1989	1990[a]
Appropriately vaccinated[a]	42	37	19
Unvaccinated	56	63	81
Vaccine indicated[b]	30	36	44
Vaccine not routinely indicated[c]	19	22[d]	31[d]
Unvaccinated for other reasons[e]	7	5	6

[a] One dose of live measles-containing vaccine on or after the first birthday.
[b] Unvaccinated persons who are ≥16 months of age without medical contraindication or exemption to vaccination.
[c] Unvaccinated persons < 16 months of age or born before 1957, persons with medical contraindication to vaccination, or persons with documentation of prior physician-diagnosed measles or serologic evidence of measles immunity.
[d] This may be an overestimate. Starting in 1989, measles vaccine was indicated routinely at 12 months of age instead of 15 months of age in many inner cities where outbreaks occurred.
[e] Unvaccinated persons who are difficult to reach, including non-US citizens and persons with religious and philosophic exemption to vaccination.

achieve, such as non-US citizens and persons with religious exemption to vaccination) (Table 2).

Nineteen percent of cases reported in 1985–1988 were in persons for whom vaccine was not routinely indicated, of which 82% were children < 16 months of age, and 30% were in unvaccinated persons for whom vaccine was indicated. In 1990, 31% of reported cases were in persons for whom vaccine was not routinely indicated[3], and 44% of all reported cases occurred in persons who were unvaccinated but for whom vaccine was indicated, the highest proportion since 1985.

Complications of Measles

The resurgence of measles in 1989–1990 had a substantial health impact. Of all reported cases, 21% had one or more complications, including 3747 (8%) with diarrhea, 2932 (6%) with otitis media, 2673 (6%) with pneumonia, and 66 (0.1%) cases of encephalitis. Nineteen percent of reported cases required hospitalization, for more than 31,000 hospital days.

Measles-Associated Deaths

From 1980 through 1988 a median of two measles-associated deaths per year were reported, for a median death-to-case ratio (DCR) of 0.64 deaths

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per 1000 reported cases. A provisional total of 41 measles-associated deaths was reported in 1989 (DCR = 2.3 per 1000 cases), and a provisional total of 89 deaths (DCR = 3.2 per 1000 cases) was reported in 1990, the largest number of deaths from measles reported in one year since 1971 and the highest DCR documented in the past 30 years. Sixty percent of reported deaths were among children < 5 years of age, including 24 (18%) less than one year of age. Twenty-eight percent of deaths were in adults over 20 years of age. Sixteen (12%) of all patients who died from measles were known to have a serious underlying illness, including seven who were known to be infected with human immunodeficiency virus. Ninety-two percent of fatal cases had no history of vaccination.

Measles Outbreaks

Measles transmission does not occur uniformly throughout the United States. Rather, it occurs in distinct outbreaks. To understand better the dynamics of measles transmission, outbreaks are classified into two major types based on the predominant age group affected (5). "Preschool" and "school-age" outbreaks are those in which children < 5 and persons 5–19 years of age, respectively, account for the greatest number of cases. Preschool outbreaks involve predominantly unvaccinated children < 5 years of age. In contrast, outbreaks among school-aged children involve highly vaccinated populations. In some large school-aged outbreaks, over 95% of cases have occurred in school-aged persons with histories of vaccination on or after their first birthday (i.e. because of vaccine failure) (5–7).

Between 1985 and 1988, 55 to 110 outbreaks occurred annually in the United States, and the major pattern was of outbreaks in highly vaccinated school-aged populations. An annual median of 47 school-aged outbreaks occurred, six of which involved > 100 persons (Table 3). These outbreaks

Table 3 Measles outbreaks in the United States, 1985–1988, 1989, and 1990[a]

	1985–1988[b]	1989	1990
Preschool-aged			
Number of outbreaks per year	8	56	106
Number of outbreaks with ≥ 100 cases	1	9	20
Proportion of total cases reported from outbreaks	20%	45%	72%
School-aged			
Number of outbreaks per year	47	170	70
Number of outbreaks with ≥ 100 cases	6	16	6
Proportion of total cases reported from outbreaks	51%	32%	10%

[a] Source: Gindler et al (8), CDC (2), CDC unpublished data.
[b] Median number, 1985–1988.

accounted for a median of 51% of all reported measles cases. From 1985 to 1988, transmission among preschool-aged children was limited, with a median of eight preschool-type outbreaks occurring annually, only one outbreak per year involving >100 persons. Preschool-aged outbreaks accounted for an annual median of 20% of reported cases during this time.

In 1989 and 1990, both the number and size of outbreaks increased, and preschool-type outbreaks became more prominent. In 1989 and 1990 a total of 248 and 239 outbreaks, respectively, were reported, and 45% and 72% of all cases, respectively, were reported from preschool-aged outbreaks (Table 3). Only 32% and 10%, respectively, occurred in school-aged outbreaks (8; CDC, unpublished data). In 1989–1990, large preschool outbreaks occurred in several inner-city areas, including Los Angeles, Houston, Milwaukee, Chicago, Dallas, and New York City. In these outbreaks, the majority of cases occurred in unvaccinated black and Hispanic children (9). Surveys in areas experiencing measles outbreaks indicate that as few as 50% of children have been vaccinated against measles by their second birthday (10), and that black and Hispanic children are less likely to be age-appropriately vaccinated than are white children (11).

CAUSES OF THE 1989–1990 RESURGENCE OF MEASLES

The measles epidemic of 1989–1990 was due primarily to widespread transmission of virus, particularly among unvaccinated preschool-aged children of racial and ethnic minority groups living in inner-city areas. Available data suggest that vaccine coverage was low in a number of cities, including some of those that experienced large outbreaks among preschool-aged children, throughout the early to mid 1980s (10).

Measles susceptibility of infants less than one year of age may also have increased. The mothers of many infants who develop measles are young, and their measles immunity may be due to vaccination rather than infection with wild virus. As a result, a smaller amount of antibody is transferred across the placenta to the fetus, compared to mothers who have higher antibody titers that result from wild virus infection. The lower quantity of antibody may wane more rapidly, making infants susceptible at a younger age today than infants in the past (12). Investigations to determine the importance of this factor are now under way.

While inadequate vaccination coverage undoubtedly contributed to the increase in measles in the United States in 1989 and 1990, it is probably not the only reason for the increase. The increase in measles in 1989–1990 was not limited to the United States. Large outbreaks of measles have been reported by many other countries of North and Central America, including Canada, El Salvador, Guatemala, Honduras, Jamaica, Mexico, and Nicaragua. The cause of this continent-wide increase in measles activity is not known. Measles vaccines appear to be as effective today as in the past. While analyses of contemporary strains of measles virus suggest that circulating viruses may have changed somewhat from past strains, vaccine-induced measles antibodies still provide a high degree of neutralizing activity against the current strains (CDC, unpublished data) as well as high clinical efficacy. For example, a 1990 study in California determined a single dose of measles vaccine to be 95% efficacious in preventing measles among preschool-aged children (13).

IMPROVING VACCINATION LEVELS AMONG PRESCHOOL-AGED CHILDREN

Outbreaks among unvaccinated urban preschool-aged children in the United States clearly demonstrate the need to increase vaccination coverage, particularly among inner-city preschool-aged children. Efforts must be intensified to increase the availability of immunization services, and to ensure that all eligible children are vaccinated whenever they present for health care. Strategies that should improve immunization levels include the following: (*a*) reducing barriers to vaccination [e.g. increasing the number of clinic hours when vaccines are given and the availability of walk-in vaccination services (14)]; (*b*) taking advantage of all opportunities to vaccinate (e.g. simultaneous use of multiple vaccines whenever possible, and excluding from vaccination only persons with valid contraindications); (*c*) using innovative vaccine delivery techniques, such as vaccination in hospital emergency departments; (*d*) increasing the number of children who return for vaccination at the appropriate age by improving follow-up and recall systems; and (*e*) targeting parents of low socioeconomic status for health education. In addition, surveys in cities experiencing outbreaks among preschool-aged children indicate that many children with measles are enrolled in assistance programs, such as the Special Supplemental Food Program for Women, Infants, and Children (WIC) and Aid to Families with Dependent Children (AFDC) (14). Projects to examine the feasibility of assessing immunization status and facilitating vaccination of children participating in entitlement programs are in progress.

VACCINATION RECOMMENDATIONS

From its introduction in 1963 until 1989, a single dose of live measles vaccine was recommended for all susceptible persons in the United States without contraindications. Persons born before 1957 are likely to have been infected with wild measles virus, and are generally considered to be immune. Since 1976, the routine age for vaccination has been 15 months because evidence showed a higher vaccine efficacy among those vaccinated at 15 months or older compared to younger children, and because the risk of infection in younger children is low in most areas of the United States (15). In urban areas where there has been a recent large outbreak of measles among preschool-aged children, recurrent transmission of measles, or where there are suspected to be large numbers of unvaccinated preschool-aged children, the first dose should be administered at 12 months of age.

Two-Dose Schedule

Most measles vaccines induce seroconversion in over 95% of susceptible children and infants. Failure to respond to measles vaccine is referred to as vaccine failure; it may either be primary (i.e. an adequate response to vaccination never developed) or secondary (i.e. an adequate response initially developed, but immunity was lost over time). The major identified risk factor for primary vaccine failure is early age at vaccination, and presumably results from interference of viral replication by persistent maternal antibody. One recent study suggests that children with mild upper respiratory illnesses, while having high seroconversion rates, are less likely to respond to measles vaccine than healthy children (16)[4]. These data have not been confirmed by other studies in developing countries (17, 18), and additional investigations are needed to determine the role of concurrent illness in measles vaccine failure. Administration of an impotent vaccine (arising from poor vaccine handling, poor administration practices, or incorrect records) may also account for some reported primary vaccine failures. However, the reason for most primary vaccine failures in persons vaccinated at 15 months of age or later is unknown. Approximately 2–5% of recipients of a single dose of live measles vaccine will fail to respond.

Serologic studies of persons who respond to vaccination indicate that measles antibody persists for many years. In addition, epidemiologic studies of outbreaks among school children and college students have found attack rates in vaccinated populations consistent with the expected primary vaccine failure rate of $<5\%$ (19). Reports of measles in persons known to have seroconverted after vaccination document that secondary vaccine

[4] Minor illness is not a contraindication to vaccination. Seroconversion rates are high, and persons who fail to respond should respond to a second dose given at the appropriate age.

failure can occur. However, this appears to be rare and probably plays only a minor role in the current epidemiology of measles in the United States.

To reduce the number of persons contracting measles because of vaccine failure, and to help prevent outbreaks of measles among such persons (e.g. in schools and colleges), the Committee on Infectious Diseases of the American Academy of Pediatrics (AAP) and the Immunization Practices Advisory Committee (ACIP) recommended in 1989 a change from a one-dose schedule to a routine two-dose schedule for measles vaccination (20, 21). Both the ACIP and the AAP recommend that the first dose of measles vaccine be routinely administered at 15 months of age in most parts of the United States. Both doses should be given as combined measles-mumps-rubella vaccine.

The recommendations of the two groups differ with regard to the age for the second dose. The ACIP recommends the second dose at school entry (4–6 years of age) while the AAP recommends the second dose at entry to middle school or junior high school (11–12 years of age). The ACIP, whose recommendations are oriented to the public sector, chose 4–6 years for the second dose primarily because of ease of implementation. Children routinely visit a health care provider before entering kindergarten or first grade to obtain booster doses of diphtheria and tetanus toxoids and pertussis vaccine (DTP), as well as oral polio vaccine. Administering the second dose of measles vaccine at the same time eliminates the need for a subsequent visit specifically for measles vaccination. The AAP chose middle school or junior high school for the second dose primarily to decrease rapidly the occurrence of outbreaks of measles among school-aged children, which occur most commonly among junior and senior high school students.

The two-dose schedule is expected to be implemented one age group at a time, although multiple age groups can be revaccinated to achieve more rapidly the goal of having children who have received two doses of vaccine in all grade levels.

New Vaccines

The resurgence of measles has demonstrated the need for early vaccination of preschool-aged children. Ideally, vaccination should take place as early in life as possible, before a child is exposed to measles. However, maternally derived antibody can interfere with an immune response to the vaccine. The high morbidity and mortality of measles among infants younger than nine months, particularly in developing countries (22, 23), has stimulated research on ways of successfully immunizing younger infants. Most studies have concentrated on the use of different vaccine strains and different vaccine doses.

Several studies have reported high seroconversion rates in infants six months of age or younger following receipt of the Edmonston-Zagreb vaccine. This vaccine virus is derived from the Edmonston strain of measles virus, but is attenuated in human diploid cells rather than in chick embryo cells, as are Schwarz and Moraten viruses. In randomized trials, the Edmonston-Zagreb vaccine has been shown to produce higher seroconversion rates than the Schwarz vaccine when administered at the same age (24, 25). The AIK-C vaccine, a vaccine produced in Japan, was also found in one study to produce higher seroconversion rates in young infants than the Schwarz strain (26).

The reasons for the differences in immunogenicity of the vaccine strains are not known. Although most published data have compared Edmonston-Zagreb with Schwarz vaccine, ongoing studies are comparing Edmonston-Zagreb with several other measles vaccine strains (27). In addition, the persistence of antibody after vaccination of young infants and vaccine efficacy are being studied. Currently, only the Moraten strain of measles vaccine is licensed for use in the United States. Studies are under way to determine the safety and immunogenicity of Edmonston-Zagreb vaccine in US infants at six months of age.

Several studies have evaluated the effect of high-dose Schwarz and/or Edmonston-Zagreb vaccine on seroconversion rates in infants (24–26, 28). These studies suggest that increasing the potency of vaccine by 10- to 100-fold produces higher seroconversion rates than standard doses, particularly when the vaccine is given in the presence of maternal antibody. While at a given dose Edmonston-Zagreb vaccine results in higher seroconversion rates than Schwarz vaccine, seroconversion rates of Schwarz vaccine administered to six-month-old Mexican infants increased from 66% with a standard dose to 91% with a 100-fold increase in dose (24). High doses of either Schwarz or Edmonston-Zagreb vaccine do not appear to be associated with an increased rate of adverse events.

Because high-titer Edmonston-Zagreb vaccine given at six months of age induces seroconversion rates equivalent to Schwarz vaccine at nine months of age[5], the World Health Organization recently changed its recommendation for measles vaccination. It now recommends that a higher-potency Edmonston-Zagreb measles vaccine be administered at six months

[5] Schwarz vaccine given at nine months of age has been recommended as the standard for the developing world.

of age in areas where measles mortality in young infants is a major health problem (27).

SUMMARY

The measles epidemic of 1989–1990 has affected predominantly unvaccinated children, particularly those of racial and ethnic minority groups residing in inner cities. Future efforts at preventing measles will need to focus on vaccinating such children at the recommended ages, 12–15 months. Prospects are promising for new vaccines that would allow vaccination at even younger ages. Implementation of the two-dose schedule for measles vaccine over the next few years should help reduce outbreaks among school- and college-aged persons.

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