

Impact of Immunizations on the Disease Burden of American Indian and Alaska Native Children

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American Indian and Alaska Native (AI/AN) people have suffered disproportionately from infectious diseases compared with the general US population. As recently as 25 years ago, rates of hepatitis A and B virus, *Haemophilus influenzae* type b, and *Streptococcus pneumoniae* infections were as much as 10 times higher among AI/AN children compared with the general US child population. In the past quarter century, routine use of childhood immunizations for hepatitis A and B viruses has eliminated disease disparities for these pathogens in AI/AN children, and significant decreases have been demonstrated for *H influenzae* type b, *S pneumoniae*, and pertussis. Nevertheless, certain infectious diseases continue to occur at higher rates in AI/AN children. The reason for continued disparities is most likely related to adverse living conditions such as household crowding, lack of indoor plumbing, poverty, and poor indoor air quality. Although tremendous strides have been made in eliminating disparities in infectious disease among AI/AN children, further gains will require addressing disparities in adverse living conditions.

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Immunization against childhood diseases is regarded as one of the greatest public health achievements in the United States and worldwide. The benefit of immunizations has been particularly notable for American Indian and Alaska Native (AI/AN) people, who have suffered disproportionately from infectious diseases compared with the general US population. Rates of infectious diseases are higher among AI/AN children than among their nonnative counterparts in the United States.¹ Although hospitalizations for infectious disease among AI/AN infants declined from 27 486 per 100 000 infants in

1988 to 14 178 per 100 000 infants in 1999, the rates for AI/AN infants from Alaska, the Southwest, and the northern plains remained higher than that for the general US infant population.¹ Major epidemics resulted in significant depopulation of some AI/AN populations,² and as recently as 25 years ago rates of hepatitis A virus (HAV)³⁻⁵

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and hepatitis B virus (HBV),⁶⁻⁸ *Haemophilus influenzae* type b (Hib),⁹⁻¹¹ *Streptococcus pneumoniae*,^{12,13} and rotavirus¹⁴⁻¹⁶ infections were as much as 10 times higher among AI/AN children than among the general US child population. Hospitalizations for lower respiratory tract infections,¹⁷ especially respiratory syncytial virus (RSV),¹⁸ in some AI/AN child populations have been 5 times those in the general US child population.

In the past quarter century, improvements in vaccine coverage for existing vaccines and introduction of new vaccines for HAV, HBV, Hib, and *S pneumoniae* have

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resulted in dramatic reductions in vaccine-preventable diseases among AI/AN people. Routine use of childhood immunizations for HBV and HAV has eliminated disease disparities for these pathogens in most AI/AN children,¹⁹ and significant decreases in disease have been demonstrated for Hib^{20,21} and *S pneumoniae*.^{22,23} Although infectious diseases in general are an important health issue for the AI/AN population, for the purposes of this article we have limited our discussion to vaccine-preventable diseases with documented higher rates among the AI/AN population compared with the US population in the prevaccine era. Because of the role of palivizumab (Medimmune, Gaithersburg, Maryland) in conferring passive immunity and overlapping risk factors for RSV and other diseases discussed, we included RSV in our review. We describe examples of the impact of vaccines in improving the health of AI/AN children through reductions in disparities in some vaccine-preventable diseases.

AI/AN DEMOGRAPHIC PROFILE

In 2004, an estimated 4.4 million people in the United States identified themselves as AI/AN alone or in combination with other races, representing 1.5% of the US population.²⁴ There are currently 562 federally recognized AI/AN tribes that represent a rich cultural and ethnic diversity. American Indian/AN people are found throughout the United States, although most AI/AN people live in the western United States. Although an increasing proportion (61%) of AI/AN people now reside in urban areas,²⁴ a significant minority still live on or near reservations or in isolated AN villages.

Compared with the non-Hispanic white population in the United States, AI/AN people historically have been at greater risk for certain infectious diseases. This increased risk for infectious diseases has been attributed to adverse living conditions, including poverty,²⁵ household crowding,²⁶ poor indoor air quality (for respiratory pathogens),²⁷ and reduced access to indoor plumbing.²⁸ American Indian/AN children who reside on reservations and in AN villages disproportionately live in crowded housing^{29,30} and lack indoor plumbing.²⁸ In addition, poverty, unemployment, low educational levels, and limited access to health care in urban settings have been cited as factors contributing to the overall poorer health status of the urban AI/AN population compared with the general US population.³¹

HEPATITIS A VIRUS

The incidence of HAV infection was substantially higher among AI/AN people than other racial/ethnic groups in the United States until the introduction of the hepatitis A vaccine (**Figure 1**).^{4,33,34} From 1990 through 1995, reported cases of HAV infection among AI/AN people accounted for 5% to 9% of all cases in the United States, although the AI/AN population constituted 1% of the total US population.³⁵ Although rates among the urban AI/AN population were several-fold higher than rates among other people living in the same areas,⁵ the overall high rates among AI/AN people were largely the result of pe-

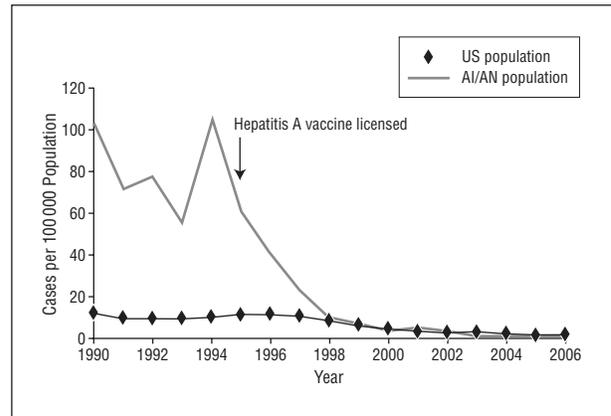


Figure 1. Incidence of hepatitis A virus infection by year (1990-2006) in American Indian and Alaska Native (AI/AN) people and the general US population. Data from Centers for Disease Control and Prevention surveillance data.³²

riodic community-wide epidemics on reservations³³ and in rural Alaskan communities.³ For example, in Alaska, these epidemics occurred every 10 to 15 years, resulting in thousands of AN people developing icteric hepatitis. During a 1992-1993 outbreak in rural Alaska, the peak reported incidence of HAV infection exceeded 2000 cases per 100 000 per year^{3,35} (**Table**). Similar periodic rates of HAV infection were documented during epidemics among AI people living on reservations.⁴

Hepatitis A vaccine was licensed in 1995 and recommended by the Advisory Committee on Immunization Practice for routine vaccination of children in populations with high rates of HAV infection, including AI/AN child populations.³⁴ Shortly after licensure, routine hepatitis A vaccination of children starting at 2 years of age was implemented nationwide in AI/AN communities as well as in states where the incidence of HAV infection exceeded 20 cases per 100 000 population. As a result, from 1997 through 2001, rates of HAV infection decreased 20-fold in AI/AN people to a level similar to the overall US rate (Figure 1).³⁵ This represents the largest decrease in the HAV infection rate that has occurred in children in the United States.³⁵

HEPATITIS B VIRUS

Chronic infection with HBV is a major cause of cirrhosis and liver failure and is a strong risk factor for the development of hepatocellular carcinoma. In the prevaccine era, 5% to 29% of AN people had serologic evidence of HBV infection.^{6,41} Before routine use of the hepatitis B vaccine, the risk of hepatocellular carcinoma among AN people chronically infected with HBV was 148-fold higher than that among their noninfected counterparts.⁷ In 1981, an evaluation of the safety and efficacy of the plasma-derived hepatitis B vaccine was conducted among AN people.⁴² Beginning in 1984, AN people received universal infant vaccination starting at birth.⁴³ In a catch-up vaccination program for AN children and adults conducted from 1984 to 1988, more than 42 000 were vaccinated.⁶ This effort, in conjunction with continued high rates of immunization in newborns and children in Alaska, resulted in a decrease in the rate of acute symptomatic HBV

Table. Rates of Individual Vaccine-Preventable Diseases in AI/AN Populations and the General US Child Population Before and After Routine Vaccination

Disease	Population (Age)	Annual No. of Cases per 100 000 Population		Postvaccine Rate Year Measured	Source
		Before Routine Vaccination	After Routine Vaccination		
HAV infection	AI/AN (all ages)	41.0-104.9 ^a	5.2 ^b	2001	Bialek et al, ³⁵ 2004
	United States (all ages)	9.1-12.7	3.9	2001	Bialek et al, ³⁵ 2004
HBV infection	AN (all ages)	215	0	1995	McMahon et al, ⁷ 1998
	United States (all ages)	10.4	1.6	2006	Wasley et al, ³⁶ 2008
Hib	AN (<5 y)	601.1	5.4	2001-2004	Ward et al, ¹¹ 1986; Singleton et al, ²⁰ 2006
	Navajo (<5 y)	152	22	1992-1999	Coulehan et al, ⁹ 1984; Millar et al, ³⁷ 2005
	White Mountain Apache (<5 y)	250	22	1992-1999	Losonsky et al, ¹⁰ 1984; Millar et al, ³⁷ 2005
IPD	United States (<5 y)	60-100	0.3	1996	CDC, ³⁸ 2002
	AN (<2 y)	403	244	2004-2006	Singleton et al, ³⁹ 2007
	White Mountain Apache (<5 y)	473	120	2001-2006	Lacapa et al, ²³ 2008
	United States (<5 y)	96.7	23.9	2003	CDC, ⁴⁰ 2005

Abbreviations: AI/AN, American Indian and Alaska Native; CDC, Centers for Disease Control and Prevention; HAV, hepatitis A virus; HBV, hepatitis B virus; Hib, *Haemophilus influenzae* type b; IPD, invasive pneumococcal disease.

^aThe rate for children younger than 5 years was 187.2 per 100 000 population.

^bThe rate for children younger than 5 years was 1.9 per 100 000 population.

infection in the AN population, from 200 per 100 000 in 1981 to less than 5 per 100 000, rates similar to those in the general US population^{43,44} (Table). Although serologic studies in AN people have documented a few breakthrough subclinical HBV infections, no children vaccinated starting at birth developed clinical HBV disease or became chronically infected through 15 years of follow-up.⁴⁵

Although the rate of acute HBV infection has decreased in young AN children, a high incidence of HBV infection has been observed among older AI adolescents and young adults in the lower 48 states, which is associated with high-risk behaviors such as injection drug use.⁸ However, little is known about the prevalence of HBV infection in AI populations in the lower 48 states because few serosurveys have been conducted.

MEASLES

Measles infections contributed significantly to morbidity and mortality among AI/AN children. In southwestern Alaska from 1960 through 1962, 44% of postneonatal deaths were caused by measles or pertussis.⁴⁶ Postneonatal mortality declined from 56.0 deaths per 1000 live births in 1960 to 1962 to 5.1 deaths per 1000 live births in 1980 to 1981, with much of this improvement attributable to the decrease in deaths due to measles or pertussis. In the 1970s, severe epidemics of measles occurred in reservations in North and South Dakota,⁴⁷ and in the 1980s a persistent outbreak of measles occurred on a reservation in Montana.⁴⁸ Studies of the Montana measles outbreak control helped to inform guidelines for outbreak control in other populations. A large measles outbreak occurred on the Navajo reservation in 1991 (S.H., unpublished data, 2008). Implementation of the 2-dose measles, mumps, and rubella vaccine recommendations led to elimination of endemic measles transmis-

sion in the United States in 2000,⁴⁹ and the current risk for measles in the AI/AN population does not appear to be higher than that for other US children.

PERTUSSIS

Pertussis infection contributed to excess infant mortality⁴⁶ and morbidity due to chronic lung disease and bronchiectasis⁵⁰ in AI/AN children. Although mortality due to pertussis among AI/AN infants decreased in the 1990s, pertussis-associated mortality remained 4 times higher in AI/AN infants than in white infants.⁵¹ Similarly, although there was a downward trend in hospitalizations for pertussis from 1980 through 2004, the 2000-2004 hospitalization rate for AI/AN children remained significantly higher than the 2003 rate for US infants.⁵²

DIPHTHERIA

Respiratory diphtheria was one of the most common causes of death among children in the prevaccine era. In Alaska, a 1925 diphtheria outbreak in Nome led to a "serum run" of diphtheria antiserum by dogsled, now commemorated by the Iditarod dogsled race. After widespread use of diphtheria toxoid vaccine in the 1940s, diphtheria became increasingly rare in the United States. However, through the 1970s, diphtheria remained endemic in some states, with reported incidence rates of more than 1.0 per 1 million population in 6 states (Alaska, Arizona, Montana, New Mexico, South Dakota, and Washington).⁵³ In 1996, after a hiatus of 20 years, 11 persons in an AI community in South Dakota were found to be infected by *Corynebacterium diphtheriae*,⁵⁴ emphasizing the importance of timely immunizations to prevent future outbreaks. Since 1997, no further cases of diphtheria have been reported in South Dakota.⁵⁵

HAEMOPHILUS INFLUENZAE TYPE b

Before the availability and public use of conjugated Hib vaccines, Hib was the leading cause of severe childhood bacterial disease, including meningitis, bacteremia, cellulitis, and epiglottitis. The incidence of invasive Hib disease was as much as 10 times higher among younger AI/AN children compared with the general US population.⁹⁻¹¹ In addition, cases of invasive Hib disease among AI/AN children occurred at a younger age than in the general US population, with 30% to 50% of AI/AN cases occurring by 6 months of age and 80% to 90% of cases occurring by 1 year of age.^{9,56,57}

The first available Hib vaccine contained the purified polysaccharide (PRP) capsule of the organism; however, use of this vaccine had little effect on Hib disease rates in US children, including AI/AN children, because most disease occurred before 18 months of age. Furthermore, this vaccine was shown to be less immunogenic among Apache Indian infants compared with infants in the general US population.⁵⁸ In the absence of an effective vaccine for infants in the early 1980s, an alternative approach using passive immunization with a hyperimmune globulin containing high concentrations of Hib anti-PRP antibodies, bacterial polysaccharide immunoglobulin (BPIG), was evaluated among White Mountain Apache infants in a double-blind placebo-controlled trial.⁵⁹ Passive immunization with BPIG conferred significant protection against invasive Hib disease during the 3 months after injection ($P = .007$). From 1989 through 2000, BPIG was effective in reducing Hib disease rates among a population of AN infants in the region with the highest rates of invasive Hib disease.⁶⁰ Development of effective Hib vaccines supplanted the need for BPIG.

In the mid-1980s, several conjugate Hib vaccines were evaluated in US children. Unlike the pure PRP vaccine, the Hib conjugate vaccines induced a T-cell-dependent response resulting in high levels of protective antibody in infants and a booster response with subsequent injections. Several of these vaccines underwent safety and immunogenicity evaluation in AI/AN populations. One of the Hib conjugate vaccines containing polyribosylribitol phosphate conjugated to the meningococcal outer membrane protein (PRP-OMP) was found to be highly immunogenic after the first dose administered at 2 months of age, an attribute essential for Hib disease prevention among AI/AN children, among whom a high proportion of disease occurred before 6 months of age.⁶¹ The PRP-OMP vaccine was evaluated in an efficacy trial in Navajo and Hopi infants and demonstrated a high level of efficacy (100%; 95% confidence interval [CI], 67%-100%) against invasive disease in children younger than 15 months who received 2 doses.⁶² In addition, between the first and second doses of vaccine, there were 8 cases in the placebo group and none in the vaccine group, resulting in a vaccine efficacy of 100% (95% CI, 41%-100%). Based on the results from this trial, PRP-OMP was licensed for use among infants in December 1990. Because of the high risk of invasive Hib disease within the first 6 months of life in many AI/AN infant populations, the Indian Health Service (IHS) and the American Academy of Pediatrics recommend that PRP-OMP Hib con-

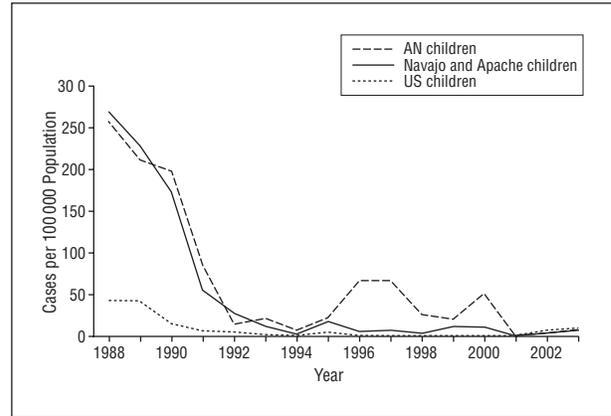


Figure 2. Incidence of *Haemophilus influenzae* type b disease by year (1988-2002) in Navajo and Apache, Alaska Native (AN), and US children younger than 5 years.^{20,21}

jugate vaccine be used for the first dose of Hib conjugate vaccine. Failure to use PRP-OMP has been associated with excess cases of Hib disease in young infants in the AN population.⁶³ Routine use of the Hib conjugate vaccine in AI/AN infants has led to a dramatic decrease in Hib disease in previously high-risk AI children in the Southwest²¹ and AN children^{20,64}; however, rates in these child populations remain higher than those in the general US child population (Table and **Figure 2**).

STREPTOCOCCUS PNEUMONIAE

With the control of invasive Hib disease, *S pneumoniae* became the most important bacterial pathogen causing meningitis, sepsis, and bacterial pneumonia. Before the use of the conjugated pneumococcal vaccine, the incidence of invasive pneumococcal disease (IPD) in certain AI/AN populations was 5 to 24 times higher than the incidence among other US children.^{12,13,65} The efficacy of a 7-valent pneumococcal conjugate vaccine (PCV 7) was evaluated in 2 pediatric populations in the United States, one of them being AI children in the Southwest. In the per-protocol analysis of the primary efficacy group (children enrolled before 7 months of age), vaccine efficacy in this population was 76.8%.⁶⁶

In 2000, the PCV 7 was licensed and routinely recommended for US infants and children and immediately implemented in AI/AN communities. Since the routine use of PCV 7 among infants and children younger than 5 years, there has been a virtual elimination of IPD by serotypes in the vaccine among AI/AN children and a significant decrease in overall disease in populations studied.^{22,39,67} For example, among White Mountain Apache children younger than 5 years, the rate of IPD from the PCV 7 serotypes decreased from 275 cases per 100 000 in 1991 through 1997 to 0 in 2004 through 2006, and the rate of overall IPD fell from 473 to 120 cases per 100 000 in these periods (Table).²³

Despite the tremendous effectiveness of the PCV 7, certain AI/AN children continue to have rates of IPD that are disproportionately high compared with those of the general US population. This is a result of the continued importance of pneumococcal serotypes not included in the PCV 7. For example, before the introduction of the PCV

7, nonvaccine serotypes (NVT) accounted for approximately 50% of IPD among Navajo children younger than 2 years and for 73% of IPD among AN children. Since the introduction of the PCV 7, the rate of IPD from NVT has remained unchanged among Navajo²² and White Mountain Apache children²³ and in most areas of Alaska, with the exception of southwest Alaska.⁶⁸ The overall annual rate of IPD has decreased in nonsouthwestern AN children younger than 5 years from 160 cases per 100 000 in 1986 through 2000 to 69 per 100 000 in 2004 through 2007.⁶⁸ However, among AN children younger than 5 years in southwest Alaska, there has been an increase in the annual rate of NVT IPD from 106 cases per 100 000 in 2001 through 2003 to 405 per 100 000 in 2004 to 2007. This regional increase in NVT IPD has diminished the overall reduction in IPD for all AN children compared with the prevaccine period from 67% in 2001 through 2003 to 39% in 2004 through 2006.³⁹ Overall rates of NVT pneumococcal disease have not changed among Navajo and White Mountain Apache populations²²; few data are available regarding IPD rates in other AI/AN populations. Despite increased rates of nonvaccine IPD, the PCV 7 vaccine is still effective in reducing IPD, and future expanded-valency vaccines should improve the vaccine-preventable proportion of IPD in high-risk AI/AN children.

ROTAVIRUS

Diarrhea is a leading cause of morbidity and mortality among children in developing countries; in the United States, diarrheal illness results in 50 000 to 70 000 hospitalizations per year.⁶⁹ In 1980 through 1982, the rate of diarrhea-associated hospitalizations in AI/AN children younger than 5 years (236 cases per 10 000 population) was nearly twice as high as the US rate (136 cases per 10 000 population).¹⁶ A large epidemic of rotavirus infections among the Apache Indian reservation documented the importance of this disease among AI populations.¹⁵ Although an updated analysis for 2000 through 2004 reveals that the hospitalization rate for AI/AN children younger than 5 years (66 cases per 10 000 population) is similar to or lower than the 2003 US rate (79 cases per 10 000), the diarrheal hospitalization rate in AI/AN infants younger than 1 year (262 cases per 10 000) remains significantly higher than the US infant rate (154 cases per 10 000).⁷⁰

From 2001 through 2004, a live pentavalent rotavirus vaccine containing 5 human-bovine reassortant rotavirus isolates was tested in a large multicenter trial that included children from the Navajo and Apache reservations. Among Navajo and Apache infants, the vaccine was found to have an efficacy of 98% (95% CI, 88.3%-100.0%) against severe rotavirus disease.⁷¹ In 2006, the Advisory Committee on Immunization Practice recommended routine vaccination of infants with pentavalent rotavirus vaccine (RotaTeq; Merck and Co, Inc, Whitehouse Station, New Jersey).⁷² During the second season of vaccination, use of this vaccine in the US child population was associated with rotavirus activity that was substantially delayed in onset and diminished in magnitude compared with previous years.⁷³ Given the demonstrated increased risk of hospitalizations for diarrheal

disease in AI/AN infants and similar efficacy among Navajo and Apache children as found in the larger US study population, use of this vaccine should decrease infant diarrheal hospitalizations in AI/AN communities.

VACCINE COVERAGE RATES

Given the high rates of some vaccine-preventable disease in the prevaccine era among many AI/AN communities, ensuring high immunization coverage is especially important. American Indian/AN children receive immunizations in a variety of settings, including IHS, tribal, and urban Indian health facilities and from other public and private health care providers. The IHS collects quarterly immunization coverage data on approximately 25 000 AI/AN children aged 19 to 35 months who are served by IHS-funded facilities, representing approximately 25% of the US Census population defined as AI/AN alone or in combination with other races in this age group. These reports show coverage that is comparable to, or higher than, coverage reported by the National Immunization Survey (NIS) for the general US population, although variation between geographic areas exists. The NIS is a random-digit-dialed survey used to monitor immunization coverage in the United States and progress toward the achievement of the Healthy People 2010 goals. An analysis of NIS data from 2000 through 2005 found that AI/AN children overall had lower immunization coverage compared with the white population in some years; sample sizes were too small to allow for analysis by geographic region.⁷⁴ In 2007, however, the NIS reported comparable coverage for AI/AN children (point estimate, 82.7%; 95% CI, $\pm 7.5\%$) and white children (77.5%; $\pm 1.3\%$) with the 4:3:1:3:3:1 vaccine series (>4 doses of diphtheria, tetanus toxoid, and any acellular pertussis vaccine, which can include diphtheria and tetanus toxoid vaccine or diphtheria, tetanus toxoid, and pertussis vaccine; >3 doses of poliovirus vaccine; >1 dose of measles, mumps, and rubella vaccine; >3 doses of Hib vaccine; >3 doses of hepatitis B vaccine; and >1 dose of varicella vaccine).⁷⁵ The IHS data reported similarly high rates (77.1% in 2008).⁷⁶ In the NIS and IHS data, coverage in the AI/AN population with most of the individual vaccines in the 4:3:1:3:3:1 series is near or above 90% (coverage with the fourth dose of the diphtheria, tetanus toxoid, and pertussis vaccine is the exception). In addition, coverage with 4 doses of PCV 7 is significantly higher in the AI/AN population (80.4%) compared with the white population (75.3%).⁷⁵ These high individual vaccine coverage rates suggest that residual disease occurring among previously high-risk AI/AN children is not a result of underimmunization. Ongoing monitoring of vaccine coverage levels, however, is needed to ensure that coverage disparities do not reemerge.

RESPIRATORY SYNCYTIAL VIRUS

Although not strictly a vaccine-preventable disease, RSV is an important health issue for the AI/AN population. Because one of the prevention strategies includes administration of palivizumab to confer passive immunity and because of overlapping risk factors with some of the vac-

cine-preventable diseases included in our review, we have included some discussion of RSV. Alaska Native infants¹⁸ and Navajo and Apache infants⁷⁷ experience extremely high rates of RSV-related hospitalization, 3 to 5 times higher than rates in the general US population. Although palivizumab has been successful in decreasing RSV hospitalization rates among premature AN infants,⁷⁸ RSV monoclonal antibodies with enhanced epitopes and future live attenuated RSV vaccines have the potential to significantly affect RSV hospitalization rates among the general AI/AN infant population.

CAUSES OF DISPARITIES

The relative impact of vaccines on specific vaccine-preventable diseases in AI/AN populations is instructive regarding the reasons for continued disparities. Some vaccine-preventable diseases, notably measles and HAV and HBV infections (in AN people), have been eliminated or occur at rates as low as, or lower than, the general US child population. These diseases have vaccines with very high efficacy (>95%) and high vaccine coverage. Other diseases such as Hib, *S pneumoniae*, and *Bordetella pertussis* infection have decreased dramatically but still occur at rates significantly higher than those of the general US child population. Vaccines for these diseases have slightly lower efficacy, allowing continued transmission to occur in adverse living conditions such as household crowding, lack of indoor plumbing, poverty, and poor indoor air quality disproportionately experienced by many AI/AN children.^{28,29} One case-control study evaluating risk factors for RSV-related hospitalization in AN children showed that household crowding was associated with a higher risk of RSV hospitalization.²⁶ Another study in a southwestern AI population demonstrated that wood-burning stoves were associated with a higher risk of respiratory illness.²⁷ High rates of skin infection, lower respiratory tract infections, and RSV hospitalizations in the AN population were associated with lack of in-home water service (running water),²⁸ and high rates of nonvaccine-type IPD in rural southwest Alaska were associated with lack of in-home running water despite complete elimination of vaccine-type IPD.⁶⁸ In addition, poverty, unemployment, low educational level, and limited access to health care may cause disparities in vaccine-preventable diseases by contributing to the overall poorer health status of the AI/AN population compared with the general US population.³¹

The driving force for excess risk of vaccine-preventable disease appears to be environmental and household factors independent of race; however, genetic risk factors cannot be excluded because conclusive studies have not been conducted. For instance, Hib and *S pneumoniae* disease rates are significantly higher in rural compared with urban AN populations,²⁰ and higher rates of *S pneumoniae* disease are associated with increased numbers of persons per household, lower per capita income, and lack of in-home running water. With 1 exception (eg, lower immunogenicity of the Hib PRP vaccine in Apache Indian children compared with other US infants⁵⁸), studies of immune responses to vaccines among AI/AN children show results comparable to those of other popula-

tions; routine vaccination has led to dramatic decreases in vaccine-preventable diseases such as HAV, HBV, and Hib infections. A near-complete absence of breakthrough infections caused by these pathogens among fully immunized AI/AN children indicates normally functioning immune responses among these populations.

CONCLUSIONS

Remarkable reductions in certain infectious diseases have occurred in the last quarter century among AI/AN child populations, driven in part by decreases in certain vaccine-preventable diseases. The use of effective vaccines has markedly decreased the health disparities from vaccine-preventable diseases between AI/AN populations and the general US child population. In addition, pioneering studies covering the epidemiology of infectious diseases, the efficacy of vaccines to prevent various infections, the impact of vaccination programs, and the long-term effectiveness of specific vaccines in the AI/AN populations have contributed to the control of infectious diseases in the United States and globally. Nevertheless, certain vaccine-preventable diseases and other infectious diseases continue to occur at higher rates in the AI/AN population compared with the general US population.

Sustained routine vaccination of all young AI/AN children will be necessary to maintain high levels of population immunity and the low disease rates currently observed in AI/AN communities. To prevent recurrence of high rates of disease in AI/AN communities, it is critical to ensure that systems for monitoring immunization coverage and conducting disease surveillance include accurate information on AI/AN populations. In addition, known risk factors for infectious disease (eg, lack of in-home water service and crowded households) need to be addressed, and additional reasons for high rates of certain infectious diseases should be investigated. Finally, studies to monitor the long-term effectiveness of vaccination programs in these populations are essential because they provide critical information on the impact of vaccines in the setting of routine use.

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