Compared with nonindigenous people, indigenous people in first-world countries have experienced much higher rates of many vaccine preventable diseases. This systematic review of published scientific literature, government reports, and immunization guidelines from Australia, Canada, New Zealand, and the United States compares pre- and postvaccination disease rates and vaccination policy for indigenous people in these four countries. Nationally funded universal vaccination programs are clearly the most effective way of reducing disease in indigenous populations. Most successful have been programs for viral diseases in which strain variations are not important and herd immunity is high, such as measles and hepatitis B. For bacterial infections, strain variations (pneumococcal disease), heavy nasopharyngeal colonization of young infants (pneumococcal and Haemophilus influenzae type b disease), low vaccine effectiveness in adults with a high prevalence of risk factors (polysaccharide pneumococcal vaccine), and waning immunity (pertussis) have been associated with continuing or widening disparities between indigenous and nonindigenous populations. However, universal vaccination programs are not always possible. Geographic targeting of all persons in certain regions with high disease rates has been successful, as has targeting of indigenous populations in regions where they constitute larger proportions of the population. In national programs targeting only indigenous people, it has been difficult to achieve high coverage, particularly in urban areas. Innovative program approaches are particularly needed in these situations.

American Native continental ancestry group; communicable diseases; Haemophilus influenzae; hepatitis; immunization; influenza, human; Oceanic ancestry group; Streptococcus pneumoniae

Abbreviations: Hib, Haemophilus influenzae type b; IPD, invasive pneumococcal disease; PRP-OMP, polyribosylribitol phosphate Neisseria meningitidis outer membrane protein.
This review summarizes the available data on the epidemiology of vaccine-preventable diseases in indigenous populations in these four countries in the context of the vaccination strategies used and their impact. The aim is to identify successful strategies with the potential for wider implementation.

METHODS

Information for this review was collected systematically by using electronic databases and government websites. Published literature was accessed through Medline (National Library of Medicine, Bethesda, Maryland) using the MeSH headings “Oceanic Ancestry Group” or “American Native Continental Ancestry Group” and “Immunization” or “Vaccines,” or any of the disease names included in this review. Internet searches were conducted for relevant publications on websites for the Australian Government Department of Health and Ageing, Health Canada, the Centers for Disease Control and Prevention (Atlanta, Georgia), and the New Zealand Ministry of Health. Specific reports used were The Health and Welfare of Australia’s Aboriginal and Torres Strait Islander Peoples (7), A Statistical Profile on the Health of First Nations in Canada (8), and Trends in Indian Health (10), as well as immunization handbooks from New Zealand, Canada, and Australia (11–13) and notifiable disease annual reports.

A major focus of this review is nationally recommended and funded vaccination schedules. Nationally recommended vaccines are funded in New Zealand (11); in the United States, childhood vaccines are funded for all indigenous children through the Vaccines for Children Program (14). In Australia, most nationally recommended childhood vaccines have been funded (13); in Canada, recommendations are made at a national level, but funding and delivery of vaccines are the responsibility of the provinces (12). The term “indigenous” in this review refers to the range of peoples who inhabited these countries prior to European colonization, that is, Native Americans, Alaskan Natives, First Nations people of Canada, Canadian Inuit, Australian Aboriginal people, Torres Strait Islanders, and New Zealand Maori.

HAEMOPHILUS INFLUENZAE TYPE B DISEASE (INVASIVE)

Epidemiology

The highest rates of invasive Haemophilus influenzae type b (Hib) disease reported in the prevaccine era were in indigenous populations (table 1), characterized by a younger age at onset (15, 16) and rarity of epiglottitis (15).

In Australia, most nationally recommended childhood vaccines have been funded (13); in Canada, recommendations are made at a national level, but funding and delivery of vaccines are the responsibility of the provinces (12). The term “indigenous” in this review refers to the range of peoples who inhabited these countries prior to European colonization, that is, Native Americans, Alaskan Natives, First Nations people of Canada, Canadian Inuit, Australian Aboriginal people, Torres Strait Islanders, and New Zealand Maori.

Vaccination schedules

The available Hib vaccines have differences relevant to the specific epidemiology in indigenous populations. The polyribosylribitol phosphate Neisseria meningitidis outer membrane protein (PRP-OMP) vaccine provides significant immune response following the first dose at 2 months of age, whereas the other conjugated vaccines (Hib oligosaccharide CRM197 and PRP tetanus toxoid) require at least two doses to reach similar levels of response (17, 18). PRP-OMP is therefore frequently recommended for indigenous populations because of their earlier average age at which Hib
disease occurs. However, PRP-OMP vaccination does not achieve as high a peak antibody concentration after a full course (19), suggesting that, compared with other vaccines, it may have less impact on nasopharyngeal carriage of Hib. Although high carriage rates have been shown in highly vaccinated populations in Alaska (20), they have not been found in comparable White Mountain Apache or Navajo populations (21).

The vaccination schedules used in the four countries are shown in table 1. All countries except Canada have had a specific role for PRP-OMP vaccine.

### Disease impact

Universal conjugate Hib vaccine programs for infants have resulted in spectacular decreases in the reported incidence of invasive Hib disease in children less than age 5 years in all four countries: by 98 percent by 1995 in the United States (21), more than 99 percent by 2000 in Canada (12), 95 percent by 2000 in Australia (22), and 92 percent by 1995–2000 in New Zealand (23). While the declines in indigenous populations were also considerable, they were less marked than in the general populations, so the relative burden in indigenous children was several orders of magnitude higher than in the general population in the United States (21), Australia (24), and New Zealand (23). Possible explanations for the continuing higher rates include earlier and heavy nasopharyngeal colonization, poorer immunologic responses due to environmental factors (25), persistent nasopharyngeal carriage (17), and delayed vaccination (20).

The reemergence of Hib disease in Alaska in 1996–1997, following replacement of PRP-OMP by a diphtheria-tetanus-whole cell pertussis–Hib oligosaccharide vaccine was replaced by a schedule including PRP-OMP vaccine for the first one or two doses. Recent data suggest that in the United States (26, 27) and New Zealand (28, 29), indigenous Hib disease incidence is approaching that in comparative populations, while in Australia (30) and Canada (8, 31) the situation is less clear (table 1). This finding provides suggestive evidence that a vaccine schedule combining initial doses of PRP-OMP vaccine to achieve early immunogenicity with booster doses of other Hib vaccines associated with higher antibody levels may be optimal for high-incidence indigenous populations.

### HEPATITIS A

#### Epidemiology

In the absence of funded vaccination programs, indigenous populations experienced higher rates of hepatitis A in all four countries (32–34), with the possible exception of New Zealand (table 2). The epidemic-related patterns ranged from hyperendemicity in young children (35) to regular community-wide epidemics in older children, including deaths (34, 36, 37).

#### Vaccination schedules

Nationally funded vaccination programs are in place in only the United States (universal childhood, since 2006) (38) and Australia (indigenous children in high-prevalence areas, since 2005) (39) (table 2). Local or regional programs targeting children in regions with large indigenous populations have previously been implemented in Canada (8) and, for indigenous children only, in the United States (36) and Australia (37).
Disease impact

Nationally and regionally funded vaccination programs, whether or not they are targeted solely at indigenous populations, have proved very effective in reducing hepatitis A in indigenous populations in the United States (36), Canada (8), and Australia (37) (table 2). Reductions in disease incidence in nontarget populations have also been seen following implementation of targeted programs (37).

**HEPATITIS B**

Epidemiology

Hepatitis B transmission in nonindigenous populations occurred predominantly in adulthood via sexual or perinatal means; in indigenous populations, infection usually occurred in early childhood, was largely asymptomatic, but led to high rates of chronic carriage and hepatic cancer (40). High rates of infection, chronic carriage, and hepatocellular carcinoma were reported in indigenous populations in all four countries before routine vaccination programs began (table 3). There appear to be some exceptions in Canada, where rates in First Nations populations were similar to those for nonindigenous populations, and a less virulent hepatitis B strain among Inuit was postulated (41).

Vaccination schedules

Vaccination strategies initially targeted infants of carrier mothers or those from ethnic or risk groups in all four countries (11, 42–44). Following the limited success of these approaches, universal infant and/or adolescent vaccination has been adopted, first in New Zealand (11) and the United States (45) (table 3).

**INFLUENZA**

Epidemiology

Little information specific to influenza in indigenous populations has been published. However, the role of influenza as a major cause of morbidity in children and morbidity and death in the elderly (48), the high frequency of secondary pneumonia (48), and high rates of morbidity and mortality due to pneumonia in indigenous populations are well documented (7, 10).

Vaccination schedules

All four countries have nationally funded vaccination programs for the elderly, but the eligible age ranges vary. Some countries include younger people with medical risk factors, and, in the United States and Canada, infants 6–23 months of age were recently included (table 4). Australia is the only country with a nationally funded program targeting indigenous adults; in Canada, younger adults are included in some provinces or territories with predominantly Inuit populations (49).
Disease impact

Data are generally not available comparing influenza and pneumonia rates in indigenous populations before and after immunization programs are implemented. However, where data are available, results show that influenza and pneumonia remain significant causes of morbidity and mortality, particularly in indigenous adults (table 4).

PNEUMOCOCCAL DISEASE (INVASIVE)

Epidemiology

Invasive pneumococcal disease (IPD) rates are highest in young children and the elderly. The rates in indigenous populations in central Australia and Alaska, White Mountain Apache, and Navajo were among the highest ever reported, for both adults and children (tables 5 and 6, respectively), but case-fatality rates were about the same as those in the nonindigenous population (50). High rates in younger indigenous adults in Australia compared with nonindigenous adults were attributed to a higher prevalence of risk factors, particularly high-risk alcohol consumption and chronic disease, and low vaccination coverage (51).

Vaccination schedules

The 23-valent polysaccharide pneumococcal vaccine includes the serotypes of an estimated 90 percent of IPD cases internationally (52), although the percentage is lower in some indigenous populations (53, 54). As with other polysaccharide vaccines, this one is poorly immunogenic in children less than 2 years of age and has no impact on mucosal carriage (52). The effectiveness of the vaccine against pneumococcal pneumonia or death from pneumococcal disease has not been established, but it has been found to be 53 percent effective in preventing IPD in immunocompetent adults (55, 56). Vaccine effectiveness against IPD in a Navajo population with high rates of alcoholism and diabetes was found to be only 38 percent in adults for vaccine serotypes, with 95 percent confidence intervals overlapping zero (53).

The currently licensed 7-valent pneumococcal conjugate vaccine is highly efficacious against IPD in infants and also has some effectiveness against pneumonia and acute otitis media (57, 58). However, the proportion of IPD that is caused by vaccine serotypes, and is therefore vaccine preventable, is lower than for 23-valent polysaccharide pneumococcal vaccine. For the 7-valent pneumococcal conjugate vaccine, the proportion is lower in indigenous (67–77 percent) compared with nonindigenous (84–86 percent) children (59–62).

Funded vaccination programs for the four countries are presented for adults in table 5 and for children in table 6. Funded polysaccharide vaccination programs for the elderly are in place in the United States, Canada, and Australia. Australia is the only country with a national program specifically for indigenous adults. Revaccination after 5 years is generally recommended only in Australia (12, 13, 63). Universal infant conjugate vaccination programs are in place in the United States and Canada; in Australia, a targeted program for indigenous infants was replaced by a universal program in January 2005 (table 6).

Disease impact

Results of polysaccharide vaccination programs for indigenous adults are mixed, consistent with low vaccine effectiveness in populations with high rates of chronic

TABLE 4. Currently funded influenza vaccination programs, and hospitalization or death rates due to influenza or pneumonia in indigenous people, before and after widespread vaccination

<table>
<thead>
<tr>
<th>Country</th>
<th>Eligible groups (reference no.)</th>
<th>Hospitalization or death rates due to influenza and/or pneumonia</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Prevaccine</td>
</tr>
<tr>
<td>Australia</td>
<td>Indigenous people ≥50 and those 15–49 years of age with risk factors; all ≥65 years of age (13)</td>
<td>N/A*</td>
</tr>
<tr>
<td>Canada</td>
<td>All &gt;65 years of age, &lt;65 years of age with risk factors‡ (49); all 6–23 months of age (89)</td>
<td>N/A</td>
</tr>
<tr>
<td>New Zealand</td>
<td>All ≥65 years of age, &lt;65 years of age with risk factors (11)</td>
<td>Hospitalizations: Maori, 9.5/100,000; nonindigenous, 7.3/100,000¶</td>
</tr>
<tr>
<td>United States</td>
<td>All ≥50 years of age; all 6–23 months of age (48)</td>
<td>Deaths: 22/100,000 (1.5 times US all-races rate)#</td>
</tr>
</tbody>
</table>

* N/A, not available.  
‡ Eligibility expanded to ≥55 years of age in Nunavut province.  
§ 1999 (8).  
¶ 1990–1999, influenza only, pneumonia not included (11).  

disease and other risk factors (table 5). Decreases in IPD rates in indigenous adults following vaccination programs have been reported from north Queensland (64) and the Kimberley (65) regions of Australia, but, in Navajo Indian adults, IPD rates were 3–5 times higher than those in the respective age groups for US Whites, notwithstanding more than 60 percent vaccination coverage (53, 66).

The impact of infant conjugate vaccination programs on IPD in indigenous children has been more impressive. The disparity between rates in Black, White, Hispanic, and other racial groups of children less than 5 years of age in the United States began to decrease before universal pneumococcal conjugate vaccination was introduced and had completely disappeared by 2002 (67). In 2003, only seven

### TABLE 5. Currently funded pneumococcal vaccination programs for indigenous adults, and disease incidence before and after widespread vaccination

<table>
<thead>
<tr>
<th>Country</th>
<th>Eligible groups (reference no.)</th>
<th>No. of cases per 100,000 per year</th>
<th>Prevaccine</th>
<th>Postvaccine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Australia</td>
<td>Indigenous people ≥50 years of age, indigenous people 15–49 years of age with risk factors; all ≥65 years of age*</td>
<td>100–180† (up to 20 times higher than for nonindigenous adults)</td>
<td>20‡</td>
<td></td>
</tr>
<tr>
<td>Canada</td>
<td>All ≥65 years of age, &lt;65 years of age with risk factors (49)</td>
<td>N/A§</td>
<td>133¶</td>
<td></td>
</tr>
<tr>
<td>New Zealand</td>
<td>None (71)</td>
<td>N/A</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>United States</td>
<td>All ≥65 years of age (63), &gt;2 years of age with risk factors (90)</td>
<td>70–190 (approximately 10 times higher than for nonindigenous adults)#</td>
<td>56 and 190**</td>
<td></td>
</tr>
</tbody>
</table>

* Indigenous adults beginning in 1999, funding for all adults ≥65 years of age beginning in 2005 (13).
† Indigenous adults ≥15 years of age in Far North Queensland, 1993–2004 (91) and in Kimberley, 1997 (65); indigenous adults 20–59 years of age in central Australia, 1985–1990 (60).
‡ Far North Queensland, 1997–2004 (91); Kimberley, 2001 (65).
§ N/A, not available.
¶ Arctic Canada, 2001, indigenous adults ≥65 years of age (92).
# ≥40 years of age; White Mountain Apache adults, 1983–1990 (50); Alaskan adults, 1986–1990 (93).
** Numbers of cases among those 18–64 and ≥65 years of age, respectively; Navajo, 1997–1998 (66).

### TABLE 6. Currently funded pneumococcal vaccination programs for indigenous children, and disease incidence before and after widespread vaccination

<table>
<thead>
<tr>
<th>Country</th>
<th>Funded vaccination program in place? (reference no.)</th>
<th>No. of cases per 100,000 per year</th>
<th>Prevaccine</th>
<th>Postvaccine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Australia</td>
<td>Yes*</td>
<td>180–2,053 (up to 15 times higher than for nonindigenous children)†</td>
<td>60–67‡</td>
<td></td>
</tr>
<tr>
<td>Canada</td>
<td>Yes§</td>
<td>225 (0 nonindigenous cases)¶</td>
<td>N/A#</td>
<td></td>
</tr>
<tr>
<td>New Zealand</td>
<td>No (71)</td>
<td>127 (107 for children of all ethnicities &lt;2 years of age)**</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>United States</td>
<td>Yes†‡</td>
<td>300–1,820, (18–52 times higher than for US nonnatives)† ‡</td>
<td>6 §§</td>
<td></td>
</tr>
</tbody>
</table>

* Indigenous infants beginning in 2001 (13), all infants beginning in 2005 (94).
† Indigenous children <2 years of age in central Australia, 1985–1990 (60); Northern Territory, 1994–1998 (54); Western Australia, 1993 (95); and Kimberley, 1995–1997 (65).
‡ Australian indigenous children <5 years of age, 2003 (68).
§ Recommended beginning in 2002 (12), funded in all provinces by 2005 (96).
¶ 2001 (92).
# N/A, not available.
†† Beginning in 2000, with catch-up for American Indians and Alaskan Natives and other high-risk children <5 years of age (90).
¶¶ <2 years of age; White Mountain Apache, 1983–1990 (50); Alaskan natives, 1980–1986 (93); and Navajo, 1996 (98).
§§ American Indians and Alaskan Native children <5 years of age, 2003 (27).
cases of IPD were notified in American Indian and Alaskan Native children less than 5 years of age, a rate slightly lower than that for Whites (27). In Australia, with only 2 years of data available on the impact of the targeted program, a slight decline in the notification rate was evident in indigenous children less than 5 years of age (68). No published data are available on the impact on otitis media, but it is likely to be less because of greater serotype diversity, greater potential for serotype switching, and early colonization (69).

OTHER VACCINE PREVENTABLE DISEASES

For measles, pertussis, and meningococcal disease, vaccination strategies have not been specifically targeted to indigenous populations. Universal two-dose childhood vaccination for measles has been implemented in all four countries (13, 70–72), and incidence has been reduced to local outbreaks related to imported cases of disease (12, 27, 30). For pertussis, universal childhood, and in some cases adolescent, programs are in place (13, 70–72). Pertussis epidemics continue to occur because of waning vaccine-induced immunity, and there have been reports of higher hospitalization (24) and notification (8) rates for indigenous infants, possibly related to delayed vaccination (24). Universal childhood vaccination for meningococcal disease was recently introduced in Canada (72) and Australia (13) and, for adolescents, in the United States (73). In New Zealand, a national 15-year epidemic of a serotype B clone has been particularly focused in Maori and Pacific Island children and has led to the development of a clone-specific vaccine and national vaccination program for all children less than 20 years of age (74), resulting in a substantial decline in reported cases (75).

CONCLUSIONS

Important lessons and points of continuity relevant to immunization programs for indigenous people in developed countries emerge from this review. First, the higher incidence and earlier age at onset of almost all diseases in all countries is consistent with adverse environmental factors, especially household crowding. Immunization programs have contributed to correcting this aspect of health inequity for indigenous people, but more needs to be done.

Nationally funded universal vaccination programs are clearly the most effective way of reducing disease in indigenous populations, as well as reducing racial disparities. The most successful have been for viral diseases in which strain variations are not important and herd immunity is high, such as measles and hepatitis B. For bacterial infections, significant reductions in disease burden have also occurred. However, strain variations (pneumococcal disease), heavy nasopharyngeal colonization of young infants (pneumococcal and Hib disease), low vaccine effectiveness in adults with a high prevalence of risk factors (polysaccharide pneumococcal vaccine), and waning immunity (pertussis) have been associated with continuing or widening of disparities between indigenous and nonindigenous populations. When conditions are not ideal, environmental factors as well as lower coverage or delayed vaccination result in limited program effectiveness. Innovative solutions, such as for Hib disease—using schedules of Hib vaccines of different antigenic composition sequentially—appear to have had a favorable impact, but, in the case of pertussis and pneumococcal disease in adults, new, more effective vaccines will likely be needed to achieve further progress.

Universal vaccination programs are not always possible. The cost-effectiveness of such programs can be limited by low disease rates in nonindigenous populations, especially for expensive vaccines. On the other hand, the high disease burden has sometimes led to vaccine trials and/or programs being implemented in indigenous populations first. However, successful wider implementation has not been limited to fully national, universal programs. Geographic targeting, in which all persons within certain regions with high disease rates are targeted, has reduced the incidence and disparities between high- and low-incidence populations for hepatitis A in the United States (36) and also for influenza in some North American regions (49). Targeting of indigenous persons in regions where they constitute larger proportions of the population has also been pursued successfully (64). Evidence from this review suggests that national programs targeting only indigenous people are the least effective approach, particularly in urban areas, where identifying indigenous people to achieve high vaccine coverage is more difficult (24). Innovative program approaches are particularly needed in these situations.

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