Invasive pneumococcal disease in Indigenous people in north Queensland, 1999–2004

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ABSTRACT

Objective: To describe the epidemiology of invasive pneumococcal disease (IPD), and the impact of pneumococcal vaccines on IPD, in Indigenous people in north Queensland.

Setting: North Queensland, 1999–2004; there are about 53 750 Indigenous people in the region, including nearly 6900 children < 5 years and nearly 5650 adults ⩾ 50 years.

Main outcome measures: Incidences of IPD in Indigenous children and in Indigenous adults compared between the 3 years before and after the introduction of a 7-valent pneumococcal conjugate vaccine (7vPCV) (1999–2001 versus 2002–2004).

Results: Estimated annual incidence of IPD in Indigenous children < 5 years of age declined from 170 to 78 cases per 100 000 in the 3 years following the introduction of 7vPCV in 2001. The annual incidence of vaccine-preventable IPD in Indigenous adults had declined by 86% since a 23-valent pneumococcal polysaccharide vaccine (23vPPV) was introduced to the region in 1996, to 15 cases per 100 000 (95% CI, 8–25) in 2002–2004.

Conclusion: Although there was a rapid decline in IPD in young Indigenous children, it is unlikely that the incidence will fall much further with the current 7-valent vaccine. There was a suggestion that vaccinating Indigenous children indirectly protected those aged 5–14 years and Indigenous adults ⩾15 years of age. Incidence of IPD in Indigenous adults in 2002–2004 was the lowest on record in the region.

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Invasive pneumococcal disease (IPD) is well recognised as an important infection in Indigenous children and adults in central and northern Australia.[1-4] In recognition of this increased risk of IPD, the 23-valent pneumococcal polysaccharide vaccine (23vPPV) was made freely available to at-risk Indigenous adults in north Queensland (defined as north of a line approximately between Mt Isa and Mackay) from 1996.[5]

Within 4 years, the estimated annual incidence of vaccine-preventable IPD in at-risk Indigenous adults in far north Queensland (defined as north of a line between Kowanyama, Croydon and Cardwell) had declined from 111 to 28 cases per 100 000.[5] However, over this time, the annual incidence of vaccine-failure IPD rose to 32 cases per 100 000. The 23vPPV was subsequently made freely available to all at-risk Indigenous adults throughout Queensland in 1998, and nationally in 1999.[5]

As Indigenous children also had increased risk of IPD,[2,4] a recently licensed 7-valent pneumococcal conjugate vaccine (7vPCV; comprising pneumococcal serotypes 4, 6B, 9V, 14, 18C, 19F and 23F) was made freely available to all Indigenous children aged under 2 years, with a booster dose of 23vPPV (at 24 months of age in Queensland) from mid-2001.[6]

We report the epidemiology of IPD in Indigenous people in north Queensland over the 3 years before, and the 3 years after, 7vPCV became available free for young Indigenous children (1999–2004). We also examine whether there was any evidence of a herd immunity effect[7] indirectly protecting either Indigenous children aged 5–14 years or Indigenous adults, in the 3 years following the introduction of 7vPCV for young Indigenous children.

METHODS

IPD is defined by the isolation of *Streptococcus pneumoniae* from a usually sterile body site; it became a notifiable disease in Queensland in 1996. Diagnostic laboratories notify local Public Health Units of each case; and, in north Queensland, Tropical Public Health Unit staff then interview each patient (or the guardian), and/or the attending physician, to complete a standardised questionnaire. This incorporates details of the case, recognised IPD risk factors and prior pneumococcal vaccination.[5]

Invasive pneumococcal isolates are forwarded to a reference laboratory for serotyping.[4]

Case definitions

An invasive isolate was defined as "vaccine type", if the serotype is included in the relevant (to the age of the patient) pneumococcal vaccine; all other serotypes were defined as "non-vaccine type".

A case of IPD was defined as "vaccine-preventable" if:

- It was in an Indigenous child who was age-eligible for free vaccine, and was caused by a 7vPCV vaccine type.
- It was in an Indigenous adult and was caused by a 23vPPV vaccine type, and the adult was eligible for free 23vPPV[8] (smoking was included among eligibility criteria for Indigenous adults from 2001[5]), or the case occurred 5 years or longer after a dose of 23vPPV.[8]

A case of IPD was defined as "vaccine failure" if it was caused by a vaccine type, and the patient had documented evidence of having received a primary course of the

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1 Average annual incidence (95% CI) of invasive pneumococcal disease (IPD) per 100 000 Indigenous people in north Queensland before and after introduction of the 7-valent vaccine in 2001

	1999–2001	2002–2004
Indigenous children		
Age < 5 years	170 (118–236)	78* (44–126)
Age, 5–14 years	36 (20–59)	15* (5–31)
Indigenous adults		
Age ⩾ 50 years	71 (37–124)	41 (6–85)
Age, 15–49 years	56 (41–75)	53 (38–71)
Vaccine-type IPD†	49 (36–65)	31*(21–45)
Vaccine preventable	19 (12–30)	15 (8–25)
Vaccine failure	23 (15–35)	13* (7–23)

* These point estimates are below the 95% CIs of the preceding 3 years. † Vaccine-type IPD = IPD caused by serotypes included in the 23-valent pneumococcal polysaccharide vaccine. ◆

relevant vaccine or the recommended booster (or revaccination)[8] more than 2 weeks before the onset of illness.[5]

Statistical analysis

Only those cases of IPD that occurred in Indigenous residents of north Queensland, and were apparently acquired in the region, were included in this report.

The incidences of IPD were calculated using population denominators from the national 2001 census; there were about 53 750 Indigenous people in the region, including nearly 6900 children aged under 5 years, about 14 010 children aged 5–14 years, and nearly 5650 adults aged 50 years or older.[9]

The differences in the numbers of vaccine type versus non-vaccine type IPD cases in the two 3-year periods were tested with the χ^2 test with Yates correction; the confidence intervals for the incidence rates were calculated using tabulated factors.[10]

Ethical approval was not necessary for this study as surveillance of communicable diseases of public health importance is required by law.

RESULTS

The annual incidence of IPD in Indigenous children and adults in 1999–2001 and 2002–2004 is shown in Box 1.

In the 3 years after the introduction of 7vPCV, there was a 54% decline (95% CI, 47%–63%) in IPD in Indigenous children aged under 5 years and a 58% decline (95% CI, 47%–75%) in those aged 5–14 years. There was also a 37% decline (95% CI, 31%–42%) in IPD caused by 23vPPV serotypes and a 43% decline (95% CI, 34%–53%) in 23vPPV vaccine failures in Indigenous adults.

2 Cases of invasive pneumococcal disease (IPD) in Indigenous people in north Queensland before and after introduction of the 7-valent vaccine in 2001

	All isolates			Non-vaccine type*			Vaccine type*		
	Total	1999–2001	2002–2004	Total	1999–2001	2002–2004	Total	1999–2001	2002–2004
Children	72	50	22	40	23	17	27	23	4
Age < 5 years	51	35	16	27†	14	13	19†	17	2‡
Age, 5–14 years	21	15	6	13	9	4	8	6	2
Adults	108	58	50	28§	9	19	79§	48	31
Age, 15–49 years	89	46	43	23	7	16	65	38	27
Age ⩾ 50 years	19	12	7	5	2	3	14	10	4

* Vaccine-type IPD = IPD caused by serotypes included in the 7-valent pneumococcal conjugate vaccine in the case of children <15 years, and the 23-valent pneumococcal polysaccharide vaccine in the case of adults ⩾ 15 years. † 46 of the 51 isolates were serotyped.
‡ Both cases were classed as vaccine-preventable. Both children were aged 3 years: one was partly vaccinated and the other unvaccinated. § 107 of the 108 isolates were serotyped. ◆

Indigenous children

There were 72 cases of IPD in Indigenous children aged < 15 years in north Queensland between 1999 and 2004.

Of the 72 cases, 51 (71%) were in children aged under 5 years (Box 2). Thirty-two of the 51 children had pneumonia (63%); 12 bacteraemia (24%); five pneumococcal meningitis (10%) with one death (serotype 6A); one had septic arthritis; and one, submandibular abscess.

Forty-six of the 51 isolates were serotyped, and 27 (59%) were non-vaccine type, with similar numbers in 1999–2001 and 2002–2004 (Box 2). The non-vaccine types were distributed among 13 serotypes, with types 1, 19A, 6A and 33F being the most common (Box 3).

Nineteen isolates were vaccine type — 17 (89%) in 1999–2001. There was a significant decline in vaccine-type IPD in Indigenous children aged under 5 years following the introduction of 7vPCV (Yates corrected $\chi^2 = 5.57$, $P = 0.02$). The two vaccine-preventable cases in 2002–2004 were both in 3-year-old children, one partly vaccinated and the other unvaccinated.

Eleven cases of IPD occurred in Indigenous children aged 2–14 years in 2002–2004, seven caused by a 23vPPV vaccine type. Six of these seven children had never received the recommended 23vPPV booster dose (scheduled at 24 months of age in Queensland). There was one 23vPPV vaccine failure (serotype 12F), in a 2.5-year-old child who had received the vaccine at 21 months of age.

There were 21 IPD cases in Indigenous children aged 5–14 years — 15 (71%) in 1999–2001 (Box 2). Eight of these 21 cases (38%) were caused by 7vPCV vaccine-type pneumococci — six in 1999–2001, and two in 2002–2004.

Indigenous adults

There were 108 cases of IPD in Indigenous adults aged ⩾ 15 years in north Queensland between 1999 and 2004 (Box 2). Of these, 89 (82%) occurred in adults 15–49 years of age, with similar numbers in 1999–2001 and 2002–2004. Seventy-one patients had pneumonia (80%), 11 bacteraemia (12%) and four meningitis; three died.

Nineteen cases were in adults aged ⩾ 50 years, with 12 (63%) in 1999–2001.

All but one of the isolates was serotyped: 28 (26%) were 23vPPV non-vaccine type

3 Distribution of non-vaccine serotypes* among invasive pneumococci isolated from children aged < 5 years in north Queensland

Serotype	1999–2001	2002–2004	Total
1	6	0	6
5	1	0	1
6A	1	3	4
7F	0	1	1
8	0	1	1
10A	0	1	1
12F	0	1	1
13	1	0	1
16F	0	1	1
17F	1	0	1
18B	1	0	1
19A	2	3	5
33F	1	2	3
Total	14	13	27

* Serotypes not included in the 7-valent pneumococcal conjugate vaccine. ◆

(nine [32%] in 1999–2001), while 79 were vaccine type (48 [61%] in 1999–2001). There was significantly more vaccine-type IPD in Indigenous adults aged ⩾ 15 years in 1999–2001 compared with 2002–2004 (Yates corrected $\chi^2 = 5.7$, $P = 0.02$).

Distribution of vaccine-type isolates is shown in Box 4. Twenty-two isolates belonged to the seven serotypes included in both 23vPPV and 7vPCV, with 16 (73%) in 1999–2001. There was a non-significant decline in IPD caused by these seven serotypes compared with all other serotypes in Indigenous adults between 1999–2001 and 2002–2004 (Yates corrected $\chi^2 = 3.28$, $P = 0.07$).

Nine (11%) of the 79 patients with vaccine-type IPD had no identified risk factor for IPD and were therefore not eligible for 23vPPV. Thirty-four of the remaining cases (49%) were classified as vaccine-preventable, with seven of these in people who had failed to receive a first 5-year revaccination. The other 36 (51%) were vaccine failures.

DISCUSSION

The annual incidence of IPD in Indigenous children aged under 5 years declined by 54% (95% CI, 47%–63%) in the 3 years after the introduction of 7vPCV. Virtually all the decline was attributable to a decline in vaccine-type IPD, providing further evidence that 7vPCV is very effective in preventing vaccine-type IPD, even in disadvantaged children.[11] However, as almost all (87%) of the IPD that occurred in these children in 2002–2004 was non-vaccine type, it is unlikely that the incidence of IPD in young Indigenous children will fall much further with the current 7-valent vaccine.

As documented previously,[4] the predominant (63%) clinical IPD syndrome in Indigenous children under 5 years of age was pneumonia. Undoubtedly, 7vPCV has prevented much bacteraemic pneumonia in vaccinated Indigenous children, but it may have also prevented a substantial burden of non-bacteraemic pneumonia in these children. In a clinical trial in the United States, 7vPCV reduced clinically diagnosed pneumonia with positive radiographic changes by 20.5%, with the greatest reduction (32%) in the first year of life.[12] The vast majority of the patients with pneumonia in that study did not have pneumococcal bacteraemia.[12] Similarly, a 9-valent pneumococcal vaccine (which also includes serotypes 1 and 5) was shown to reduce radiologically confirmed pneumonia by 20% in HIV-negative children in South Africa, after a three-dose primary series in infancy and no booster.[13]

We also observed a 58% decline (95% CI, 47%–75%) in the incidence of IPD in Indigenous children aged 5–14 years from 1999–2001 to 2002–2004. Although the small number of cases precludes any certainty, it is quite possible that a herd immunity effect, with vaccinated young Indigenous children indirectly protecting their older siblings,[7] is involved. A recent decline in IPD in people aged 5–17 years, presumably a similar older sibling herd immunity effect, has recently been reported from the United States.[14]

It is of interest that serotypes 6A and 19A were the leading non-vaccine types causing IPD in Indigenous children under 5 years of age in 2002–2004, as these two serotypes are closely related to the vaccine serotypes 6B and 19F, respectively. All six young Indigenous children with IPD caused by serotype 6A or 19A had received some 7vPCV, with four having completed a three-dose primary series (data not shown). Post-licensure surveillance has raised concerns about cases of serotype 19A IPD occurring in vaccinated children in the US,[15,16] and an epidemiological study was not able to demonstrate any cross-protection against 19A.[17] Although it did demonstrate cross-protection against serotype 6A,[17] laboratory studies suggest that this cross-protection does not have optimal functional activity,[18] possibly explaining why serotype 6A has persisted among vaccinated Indigenous children in north Queensland.

There was also a significant decline in vaccine-type IPD in Indigenous adults between 1999–2001 and 2002–2004, but no significant decline in IPD caused by the 7vPCV serotypes, suggesting that there was no indirect herd immunity effect following the vaccination of Indigenous children.

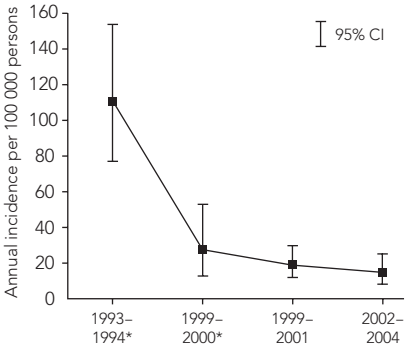
However, there was clearly an outbreak of IPD caused by serotype 1 affecting Indigenous people in north Queensland in 1999–2001 (Boxes 3 and 4). Of the 24 serotype 1 isolates identified between 1999 and 2004, 19 occurred in 1999–2001, with 15 of these in Indigenous people. Outbreaks of serotype 1 disease have been previously

4 Distribution of vaccine serotypes among invasive pneumococci isolated from Indigenous adults ⩾ 15 years of age in north Queensland

Serotype	1999–2001	2002–2004	Change
Serotypes in both vaccines*			
4	4	1	–3
6B	1	0	–1
9V	3	2	–1
14	2	2	0
18C	2	1	–1
19F	3	0	–3
23F	1	0	–1
Total	16	6	–10
23vPPV-only serotypes			
1	7	1	–6
3	3	3	0
5	3	0	–3
7F	7	7	0
8	2	5	+3
10A	1	1	0
11A	2	1	–1
12F	2	2	0
19A	4	2	–2
22F	0	3	+3
33F	1	0	–1
Total	32	25	–7
All vaccine serotypes	**48**	**31**	**–17**

* Serotypes included in both the 7-valent (7vPCV) and 23-valent (23vPPV) vaccines. ◆

5 Annual incidence of vaccine-preventable invasive pneumococcal disease in Indigenous adults aged ⩾ 15 years



* Data for the two earlier periods were from far north Queensland.[5] ◆

reported among disadvantaged communities, including Aboriginal Australians.[19,20]

Excluding all the serotype 1 cases, there was then a significant reduction in IPD caused by serotypes included in both 23vPPV and 7vPCV compared with all other serotypes in Indigenous adults between 1999–2001 and 2002–2004 (Yates corrected $\chi^2 = 4.50$, $P = 0.03$). This suggests that the serotype 1 outbreak obscured an indirect herd immunity effect, which protected Indigenous adults following the introduction of 7vPCV for Indigenous children from the latter part of 2001. A similar herd immunity effect protecting adults from IPD was observed following the introduction of 7vPCV for children in the US.[15,17]

Although the decline in vaccine-preventable IPD in Indigenous adults between the two periods was not significant, there has been a continued decline since 23vPPV was first used in Indigenous adults in the region from 1996 (Box 5). The continued downward trend is very encouraging, and suggests that there is not only high vaccine coverage among at-risk Indigenous adults in the region,[5] but also that the vaccine is effective in this population. If the latter is correct, it is in marked contrast to the finding that 23vPPV was not effective in preventing vaccine-type IPD in a population of Native American adults in the US.[21]

Also encouraging was the significant decline in IPD vaccine failures in Indigenous adults between the two periods. This may reflect the reduced transmission of serotype 1 and the 7vPCV vaccine types, but it may also be a consequence of revaccination with 23vPPV, as many of the Indigenous adults vaccinated for the first time from 1998 onwards would have been eligible for revaccination from 2002. However, a relative immune hyporesponsiveness follows revaccination, and there are very limited data on the protection following revaccination with 23vPPV.[22] Regardless, it does not appear that revaccination with 23vPPV is associated with an increased risk of adverse events significant enough to require medical review.[23]

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COMPETING INTERESTS

Jeffrey Hanna has received honoraria and travel grants from vaccine manufacturers, including Merck Sharp and Dohme and Wyeth.

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