# Impact of conjugate *Haemophilus influenzae* type b (Hib) vaccine introduction in South Africa

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**Objective** To analyse trends in reported invasive *Haemophilus influenzae* disease in South Africa within the first five years of introduction of conjugate *Haemophilus influenzae* type b (Hib) vaccine in the routine child immunization schedule.

**Methods** We used national laboratory-based surveillance data to identify cases of invasive *H. influenzae* disease between July 1999 and June 2004, and submitted isolates for serotyping and antimicrobial susceptibility testing.

**Findings** The absolute number of Hib cases (reported to the national surveillance system) among children below one year of age decreased by 65%, from 55 cases in 1999–2000 to 19 cases in 2003–04. Enhanced surveillance initiated in 2003, identified human immunodeficiency virus (HIV)-infection and incomplete vaccination as contributing factors for Hib transmission. The total number of laboratory-confirmed cases of *H. influenzae* remained unchanged because non-type b disease was being increasingly reported to the surveillance system concomitant with system enhancements. Children with non-typable disease were more likely to be HIV-positive (32 of 34, 94%) than children with Hib disease (10 of 14, 71%), $P = 0.051$. Recent Hib isolates were more likely to be multidrug resistant (2% in 1999–2000 versus 19% in 2003–04, $P = 0.001$).

**Conclusion** Data from a newly established national laboratory-based surveillance system showed a decrease in Hib disease burden among South African children following conjugate vaccine introduction and identified cases of non-typable disease associated with HIV infection.

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## Introduction

Use of conjugate vaccines for the prevention of *Haemophilus influenzae* type b (Hib) disease in children has substantially decreased the burden of disease in developed[1–3] and developing countries.[4–7] These vaccines are highly effective against invasive disease and may prevent up to 25% of radiographically confirmed pneumonia,[8–10] but are not used in some developing countries due to their high cost and because Hib remains under-recognized as a cause of severe disease and death.[11] The vaccine-preventable burden of Hib disease is likely to be greater among HIV-infected than among uninfected children due to much higher rates of Hib disease.[12] The vaccines have, however, been less effective in HIV-infected children,[13–14] highlighting the need for evaluation of the impact of vaccine introduction in populations with a high burden of HIV infection.

South Africa was the first country in Africa to self-finance and incorporate the Hib vaccine into its routine child immunization schedule from July 1999. It concurrently established a national laboratory-based surveillance for invasive Hib disease to document the impact of routine vaccination on Hib disease.[15] We analysed data from this surveillance system for the first five years to document changes in the number of reported cases of laboratory-confirmed *H. influenzae* disease among children less than five years old in South Africa.

## Methods

South Africa introduced the Hib vaccine (Tetramune, Wyeth Lederle Vaccines and Pediatrics) in March 1998 as part of a pneumococcal conjugate vaccine trial in Soweto (urban black community with 120 000 children less than five years old in 1995), Gauteng province, affecting a total of 19 267 children.[14] Population-based studies in South Africa had previously demonstrated rates of invasive Hib disease of 170 per 100 000 infants below one year of age.[14,16] National population estimates for children less than five years old in 2002 were 4 455 000, and in Gauteng and Western Cape (from where majority of the disease is reported) 737 600 and 409 600, respectively.

### National laboratory-based surveillance system

The surveillance system defined invasive *H. influenzae* and *Streptococcus pneumoniae* disease as isolation of the organisms from normally sterile body fluids of South Africans of all ages.[15] All clinical laboratories in South Africa were

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requested to report cases of invasive *H. influenzae* infection and send isolates to the central reference laboratory at the Respiratory and Meningeal Pathogens Research Unit, National Institute for Communicable Diseases (NICD) (branch of the National Health Laboratory Service (NHLS)) in Johannesburg. We excluded isolates from the same disease episode.

Clinical laboratories routinely culture specimens of blood and cerebrospinal fluid for isolation of bacteria, although before this time, no nationwide system existed for reporting cases or collecting isolates. The number of clinical laboratories reporting cases increased during each year of our study period — 80 laboratories during July 1999–June 2000 to 88, 91 and 103 in 2000–01, 2001–02 and 2002–03, respectively. We observed no deterioration in laboratory standards. The surveillance system was enhanced in 2003 by placing additional surveillance staff in 15 hospitals in seven of nine provinces, thereby increasing the number of reporting laboratories to 126 in 2003–04. From 2003, we reviewed cases at sentinel sites throughout the country for outcome, HIV status (based on serology for all ages and serology with clinical features and/or positive polymerase chain reaction (PCR) results for children less than 18 months old) and vaccination history. Laboratories were encouraged to report all cases of laboratory-confirmed disease even if no isolates were available. Annual regional laboratory audits identified 54 laboratory-confirmed cases of *H. influenzae* among all ages during the study period (24, 5, 12, 9 and 4 cases per 12-month interval) that were not reported to the NICD, suggesting that approximately 70% of all laboratory-confirmed *H. influenzae* infections were reported. We added the cases identified by audit to the surveillance database.

### Hib conjugate vaccine

The vaccine was part of a combination product (CombActHIB, Aventis Pasteur) containing diphtheria toxoid, tetanus toxoid and whole cell pertussis antigen (DTwP) for children receiving their first dose of diphtheria–tetanus–pertussis vaccine. The vaccine was prepared by reconstituting dried Hib conjugate powder with DTwP as diluent. The recommended dosage schedule was at six, 10 and 14 weeks without booster. There was no catch-up schedule for vaccinating children who had already received their first dose of DTwP. We experienced sporadic shortages of the combination vaccine from 1999 through 2002.

### Identification of isolates

We identified isolates with the γ-aminolaevulinic acid (ALA)-porphyrin test reaction and API NH (bioMérieux sa, Marcy-l'Etoile, France).[17] Slide agglutination for serotyping was performed using agglutinating sera for types a–f (Murex Biotech Ltd, Dartford, Kent, England). Serotyping results for all isolates were confirmed by PCR.[18] Cases without isolates were excluded from further analysis. Susceptibility testing was performed according to Clinical and Laboratory Standards Institute guidelines.[19] Minimum inhibitory concentrations were determined by Etest (AB Biodisk, Solna, Sweden) for isolates not susceptible (intermediately resistant and resistant) to any antibiotic. Nitrocefin was used to test for β-lactamase production. Multiple drug-resistant isolates were isolates not susceptible to ampicillin, chloramphenicol and trimethoprim-sulfamethoxazole.

### Analyses

The mean age of children less than five years old for each 12-month period was compared using the nonparametric Kruskal–Wallis test. Percentage decreases were calculated by comparing the number of reported cases in July 1999–June 2000 with cases reported in July 2003–June 2004. Rates of reported cases of invasive Hib disease were calculated for 12-month periods from 1 July to 30 June of the following year. Numerators were the number of viable *H. influenzae* isolates confirmed as serotype b at the reference laboratory. Denominators were mid-year population estimates obtained from the South African Health Information Systems Programme. We obtained vaccine coverage data from the Department of Health[20] and Health Systems Trust,[21] and HIV seroprevalence estimates from antenatal clinic surveys.[22,23] We used $\chi^2$-test to analyse trends in the proportion of antimicrobial resistant isolates over the five periods and managed and analysed data using Epi Info software, version 6.04d.[24]

## Findings

In our study, 920 cases of invasive *H. influenzae* disease were reported to the surveillance system from July 1999 to June 2004 for all ages; 847 (92%) provided the patient's age. Of the 920 isolates, 712 (77%) were recovered for serotyping and antimicrobial susceptibility testing. With the increased number of surveillance audits through the period, we identified an increasing number of laboratory-confirmed cases retrospectively for which no isolates were available. Cases with isolates therefore decreased from 84% during 1999–2000 to 74% during 2003–04, with a significant downward trend over the five-year period ($P$ = 0.02). Of the 712 viable isolates, 300 (42%) were serotype b (109, 61, 43, 44 and 43, respectively, for the five periods), 104 (15%) were other capsular types and 308 (43%) were unencapsulated *H. influenzae*.

Among cases for which the patient's age was known, 218 (78%) of 279 Hib isolates and 225 (61%) of 370 other *H. influenzae* isolates were among children less than five years old (Table 1). Of Hib cases aged five years and above, 16 (6%) occurred among those aged 5–9 years, 5 (2%) among those aged 10–14 years and 40 (14%) among adults aged 15 years or more. We found that reported cases of invasive disease among children less than five years old caused by Hib decreased substantially during the five-year period, while those caused by *H. influenzae* other than Hib and *S. pneumoniae* increased to more than twofold (Table 1). Among children less than five years old with invasive Hib disease, 60% (130 cases) occurred among those below one year (Table 2), 13% (29) among those aged 12–17 months and 27% (59) among those aged 18 months or more. We noted no significant change in the median age (9 months) of Hib cases among children less than five years old ($P$ = 0.162) during the entire study period. We found positive cultures from cerebrospinal fluid specimens (with or without other specimens) for over half of these cases (113, 52%), from blood specimens for 104, and from a pleural fluid specimen for one case. We found no reported cases of epiglottitis.

Our analyses revealed that Hib cases decreased by 65% among children less than one year old (55 cases in 1999–2000 to 19 in 2003–04) (Table 3). In Gauteng, Hib cases decreased from 20 to 10, and in the Western Cape from 12 to 2, during the same time period. In Gauteng and Western Cape, rates of reported Hib disease among children below one year decreased by 57% (13.1

Table 1. **Reported cases of invasive disease caused by *Haemophilus influenzae* and *Streptococcus pneumoniae* in South African children less than five years old, by 12-month period**

| Disease | Years of surveillance | | | | | |
|---|---|---|---|---|---|---|
| | 1999–2000 | 2000–01 | 2001–02 | 2002–03 | 2003–04 | % change[a] |
| | *n* (%) | | | | | |
| *Haemophilus influenzae* | | | | | | |
| Type b | 89 (65) | 43 (46) | 27 (30) | 33 (31) | 26 (17) | –71 |
| Other typable[b] | 8 (6) | 6 (6) | 11 (12) | 13 (12) | 25 (16) | 213 |
| Nontypable | 18 (13) | 19 (20) | 32 (35) | 35 (33) | 58 (37) | 217 |
| No isolate available | 22 (16) | 26 (28) | 21 (23) | 25 (24) | 46 (30) | Not applicable |
| All | 137 | 94 | 91 | 106 | 155 | 12 |
| *Streptococcus pneumoniae* (all serotypes) | 453 | 691 | 788 | 733 | 1218 | 169 |

[a] Comparing 1999–2000 with 2003–04.
[b] Includes serotypes a ($n$ = 10), c ($n$ = 6), d ($n$ = 5), e ($n$ = 3) and f ($n$ = 39).

cases per 100 000 in 1999–2000 versus 5.7 per 100 000 in 2003–04; 95% confidence interval (CI): 8–80%, $P$ = 0.04), and 85% (14.6 versus 2.2 cases per 100 000; 95% CI: 32–97%, $P$ = 0.010), respectively (Table 3).

We also found a 79% decrease (from 34 to 7 cases) in national recording of invasive disease among children 1–4 years of age (Table 3). The decrease in this age group was also evident in Gauteng and Western Cape (13 to 5 cases and 16 to 1 case, respectively). Our analyses of antenatal HIV seroprevalence rates among pregnant women showed that rates during 2000–04 increased in Gauteng (from 29% to 33%) and Western Cape (from 9% to 15%) (Table 3).

We found that all ampicillin-resistant Hib isolates produced β-lactamase. Although the number of Hib cases decreased during the final surveillance year, isolates of Hib were more likely to be ampicillin resistant (8 (31%) of 26 cases in 2003–04 versus 14 (16%) of 89 isolates in 1999–2000; $P$ = 0.036, $\chi^2$-test for trend) (Fig. 1). In addition, even though the absolute number of cases decreased over the years, the proportion of multiple drug-resistant isolates increased by 2%, 7%, 15%, 15% and 19% for each 12-month period respectively ($P$ = 0.001, $\chi^2$-test for trend).

Before the introduction of the Hib conjugate vaccine, a national survey of vaccination coverage in 1998 estimated that 72% of infants had received three doses of DTwP by one year of age.[20,21] Annual coverage figures based on routine clinic reports of vaccinations estimated that 64% of South African children were fully immunized (three doses of DTwP and Hib) by one year of age in 2000, 72% in 2001 and 68% in 2002. Provincial estimates for Gauteng were lower for 2002 at 61%, but similar to the national estimates for the other two years. In Western Cape 79%, 73% and 56% were immunized in 2000, 2001 and 2002, respectively.

During the 18 months of enhanced surveillance (January 2003–June 2004), 212 *H. influenzae* cases were reported nationally among children less than five years old (44/154 (28%) of these confirmed cases of Hib); 114 (54%) at sentinel hospitals (18/82 Hib (22%), 46 nontypable, 18 other than serotype b cases, and 32 cases with no viable isolates). Vaccination status was available for 15 Hib cases, four of whom were too young to be immunized, one five-month-old child was unimmunized and 10 received at least one dose of Hib vaccine. A nine-month-old HIV-uninfected child who had received a third dose of the Hib conjugate vaccine four months before presenting with Hib meningitis, subsequently died. HIV status was documented for 15 cases: 11 (73%) were HIV-infected, including five of eight cases less than one year of age.

Table 2. **Reported *Haemophilus influenzae* serotype b (Hib) disease among South African children less than five years old, by age group and 12-month period**

| Age group | Years of surveillance | | | | |
|---|---|---|---|---|---|
| | 1999–2000 | 2000–01 | 2001–02 | 2002–03 | 2003–04 |
| Reported Hib cases[a] (all age groups) | 89 | 43 | 27 | 33 | 26 |
| <6 weeks | 2 | 2 | 1 | 2 | 3 |
| 6 weeks to <1 year | 53 | 24 | 14 | 13 | 16 |
| >14 weeks[b] to <1 year | 43 | 20 | 13 | 10 | 14 |
| 1 to <2 years | 21 | 8 | 6 | 4 | 5 |
| 2 to <3 years | 9 | 9 | 4 | 4 | 0 |
| 3 to <4 years | 2 | 0 | 2 | 5 | 2 |
| 4 to <5 years | 2 | 0 | 0 | 5 | 0 |

[a] Excludes 21 cases reported without exact age specified: 4, 6, 6, 2 and 3, respectively by 12-month period.
[b] Vaccination schedule for three doses of Hib conjugate vaccine: 6, 10 and 14 weeks of age.

Table 3. **Number and rates of reported cases of invasive *Haemophilus influenzae* serotype b disease in children less than five years old in Gauteng and Western Cape provinces and South Africa as a whole, by 12-month period**

| Region and age group | Years of surveillance | | | | | |
|---|---|---|---|---|---|---|
| | 1999–2000 | 2000–01 | 2001–02 | 2002–03 | 2003–04 | Total |
| **South Africa** | | | | | | |
| <1 year (cases/100 000) | 55 (6.2) | 26 (2.9) | 15 (1.7) | 15 (1.6) | 19 (2) | 130 |
| 1–4 years (cases/100 000) | 34 (0.9) | 17 (0.5) | 12 (0.3) | 18 (0.5) | 7 (0.2) | 88 |
| HIV[a] seroprevalence rates (%) in antenatal clinic attendees | 24.5 | 24.8 | 26.5 | 27.9 | 29.5 | |
| Number of laboratories reporting nationally | 80 | 88 | 91 | 103 | 126 | |
| **Gauteng Province** | | | | | | |
| <1 year (cases/100 000) | 20 (13.1) | 11 (7.0) | 5 (3.1) | 8 (4.7) | 10 (5.7) | 54 |
| 1–4 years (cases/100 000) | 13 (2.4) | 9 (1.6) | 6 (1.1) | 11 (1.9) | 5 (0.9) | 44 |
| HIV seroprevalence rates (%) in antenatal clinic attendees | 29.4 | 29.8 | 31.6 | 29.6 | 33.1 | |
| **Western Cape Province** | | | | | | |
| <1 year (cases/100 000) | 12 (14.6) | 6 (7.1) | 5 (5.8) | 2 (2.3) | 2 (2.2) | 27 |
| 1–4 years (cases/100 000) | 16 (5.1) | 4 (1.3) | 5 (1.6) | 3 (0.9) | 1 (0.3) | 29 |
| HIV seroprevalence rates (%) in antenatal clinic attendees | 8.7 | 8.6 | 12.4 | 13.1 | 15.4 | |

[a] HIV = human immunodeficiency virus.

Among four cases who had received one or more Hib vaccine dose and were of known HIV-status, three (75%) were HIV-infected. Clinical outcomes were reported for 29 cases since January 2003, five (17%) of whom died.

We observed that nationally over the five years, the median age for nontypable disease ($n$ = 162) and disease due to serotypes other than serotype b ($n$ = 63) among children less than five years old did not change (median age 10 months for both groups). During the period of enhanced surveillance, children with nontypable disease were more likely to be HIV-positive (32 of 34, 94%) than those with Hib disease (10 of 14, 71%), $P$ = 0.051. All children who had serotypes other than b (12 of 12) were HIV positive.

## Discussion

In South Africa, a national laboratory-based surveillance for invasive Hib disease demonstrated a significant decrease in cases of invasive disease following the introduction of Hib conjugate vaccine into the routine child immunization schedule. While surveillance data did not provide an accurate estimate of the true burden of Hib disease due to limitations of the reporting system, the demonstration of vaccine impact at the national level is important given the decision to provide this relatively expensive vaccine for all South African children. The cost benefits of administering this vaccine to a 1992 Cape Town birth cohort ($n$ = 46 537) was between US$ 0.8 million and US$ 1.2 million.[25] Our findings are especially important given the high prevalence of HIV in the country.

Although the laboratory reporting system in South Africa may underestimate the incidence of Hib disease among children less than five years old, we believe the decrease in Hib disease is a minimum estimate of the full impact of the vaccine in South Africa. Population-based studies conducted in Soweto (Gauteng province) in 1997–98 and Cape Town (Western Cape province) in 1991–92 (before the introduction of Hib vaccine) identified annual incidences of invasive Hib disease of approximately 170 cases per 100 000 children below one year.[14,16] These rates were much higher than those detected by our surveillance in these two provinces during July 1999–June 2000 — 13.1 and 14.6 cases per 100 000 children below one year. In Gauteng, the vaccine had been administered to Soweto children since 1998, and since our surveillance system was established at the time of vaccine introduction (i.e. July 1999) the initial rates of Hib disease are likely to reflect some impact of the immunization. Moreover, the pre-immunization studies were performed at academic hospitals where specimens are routinely collected for diagnostic purposes and laboratories are well-equipped. We have seen improvements in case ascertainment throughout the country reflected in the increase in isolates of nontype b *H. influenzae* and *S. pneumoniae*. In addition, shortages of vaccine were reported during the first years. Thus, we believe that data from the national surveillance are likely to underestimate the impact of Hib vaccine and that the 65% decrease in cases among children below one year during the study period should be interpreted as a minimum estimate.[3,26]

In South Africa, national estimates suggest that 8% of 1.1 million children born in 2002 were infected with HIV at birth or through breastfeeding during their first year of life.[27] Our analysis revealed that the decrease in Hib disease was lower in Gauteng, where HIV seroprevalence rates were more than twice that in Western Cape. HIV infection was very common among Hib cases at sentinel sites. Lower vaccine effectiveness and increased susceptibility to Hib disease among HIV-infected children may contribute to the persistent low rates of Hib disease in South Africa.[13,14] Further studies are needed to determine the relative importance of these two factors. With antiretroviral therapy decreasing mortality and progression to AIDS among infants,[28] and its implementation in Africa showing promising

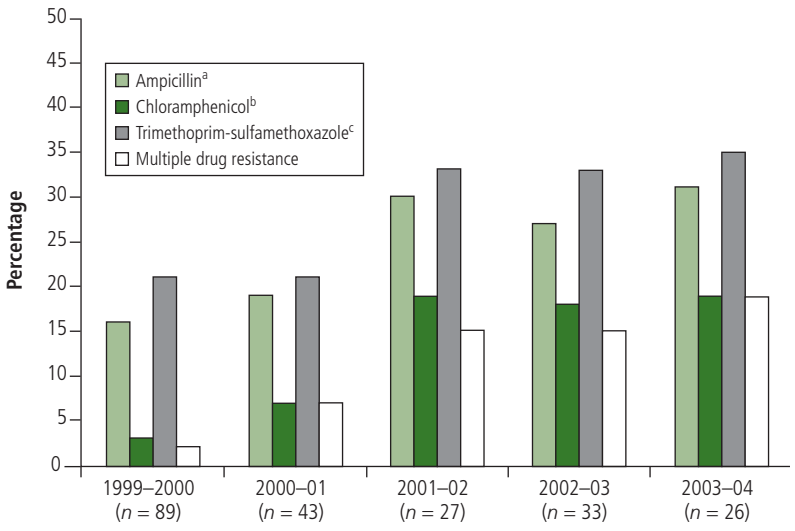
results,[28,29] it will become more common in paediatric care in South Africa.[30] Thus, monitoring of Hib disease may influence decisions to include additional doses of Hib and other vaccines for HIV-infected children.[31]

We observed an increase in reported cases of non-Hib disease possibly due to improved quality of surveillance, which is supported by the increase in reported pneumococcal disease over the same time period. These diseases may however also be increasing due to increases in the number of persons living with HIV infection. Data from a small number of cases from sentinel sites showed that HIV infection was more common among paediatric cases of *H. influenzae* due to nontypable strains than among cases of Hib. Another explanation may be replacement disease, although it has not been significant in other parts of the world,[32,33] HIV-coinfection may contribute to other strains filling the niche previously occupied by Hib. Our data do not allow us to distinguish between the relative contributions of these factors to the observed increase.

The reported coverage with the three doses of Hib vaccine in South Africa was less than that described in developed countries,[26,34] although several limitations with regard to both numerator data and population denominators hamper accurate coverage estimates.[20,21] We were unable to obtain sufficient data to determine the true incidence of vaccine failures. Failure after complete vaccination among children 14 weeks old or above was recorded for only one child. We believe that obtaining better data on vaccination histories will be necessary to determine the role of vaccine failure among infants presenting with Hib disease.[35–37] South Africa uses an accelerated schedule for Hib vaccine at six, 10 and 14 weeks without a booster dose,[15] which might increase disease prevalence among older children due to waning immunity.[35,38] In the last year of surveillance (2003–04) however, only seven of 26 cases of Hib disease (for whom age was recorded) occurred after the age at which a booster may be given (i.e. children more than one year old).

We believe that the use of national surveillance data has several important limitations. The true burden of potentially preventable Hib disease may be significantly higher than that observed by culture-confirmed disease alone.[8–11]

Fig. 1. **Proportion of non-susceptible isolates causing *Haemophilus influenzae* serotype b disease in children below five years, by category for each of the 12-month periods, South Africa**




[a] $\chi^2$ - test for trend, $P = 0.04$.
[b] $P = 0.001$.
[c] $P = 0.06$.

We included calculated rates of Hib disease only for cases where viable isolates could be confirmed as type b and for which the age of the patient was known. We did not adjust for the increase in the number of reporting laboratories, or the impact of enhancements made to the surveillance system in 2003, both of which likely increased the number of Hib cases identified. The low number of cases from many provinces may be due to several factors, including low accessibility to health care in rural areas, reduced numbers of blood cultures being taken per patients admitted,[39] smaller rural laboratories not having resources for diagnosis unless as part of studies[40] and underreporting of diagnosed cases by the laboratory to the surveillance unit. Although laboratory-confirmed Hib cases are notifiable to the Department of Health in South Africa since 1999, notification remains uncommon and no cases were identified through the national reporting system during our five-year study period.

## Conclusion

The inclusion of the Hib conjugate vaccine in the child immunization schedule is justified in the face of the HIV epidemic which affects a large number of newborns. Increasing antibiotic resistance among Hib isolates in our population[12,41] is an additional justification for vaccine introduction. In the future, better information about underlying conditions and vaccine status together with a carefully planned case-control study will assist decision-makers and public health experts in understanding the possible reasons for the transmission of Hib disease among children in South Africa. This may be especially important with the increasing survival of young children with HIV-infections due to the recent introduction of comprehensive care including antiretroviral therapy. ■

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**Competing interests:** none declared.

## Résumé

### Effet de l'introduction du vaccin conjugué anti-*Haemophilus influenzae* type b (Hib) en Afrique du Sud

**Objectif** Analyser les tendances observées dans les infections invasives à *Haemophilus influenzae* en Afrique du Sud pendant les cinq premières années suivant l'introduction du vaccin conjugué anti-*Haemophilus influenzae* type b (Hib) dans le calendrier de vaccination systématique de l'enfant.

**Méthodes** On a utilisé les données de la surveillance nationale au laboratoire pour définir les cas d'infection invasive à *H. influenzae* entre juillet 1999 et juin 2004 et soumis des isolements au sérotypage et à des épreuves de sensibilité aux antimicrobiens.

**Résultats** Le nombre absolu de cas d'infection à Hib (notifiés au système de surveillance national) chez l'enfant de moins d'un an a diminué de 65 %, passant de 55 en 1999-2000 à 19 en 2003-2004. Le renforcement de la surveillance commencé en 2003 a permis de constater que l'infection par le virus de l'immunodéficience humaine (VIH) et la vaccination incomplète constituaient des facteurs contribuant à la transmission du Hib. Le nombre total de cas d'infection à *H. influenzae* confirmés au laboratoire est resté inchangé, les infections n'appartenant pas au type b étant de plus en plus notifiées au système de surveillance à mesure que celui-ci devenait plus performant. Les enfants touchés par une infection à *Haemophilus* de type impossible à déterminer étaient plus souvent VIH-positifs (32 sur 34, 94 %) que les enfants infectés par Hib (10 sur 14, 71 %, p = 0,051). On a également observé une probabilité plus grande de multirésistance dans les isolements récents de Hib (2 % en 1999-2000 contre 19 % en 2003-2004, p = 0,001).

**Conclusion** Les données issues d'un système national de surveillance au laboratoire récemment mis en place ont fait apparaître une diminution de la charge de morbidité due à Hib chez les enfants sud-africains à la suite de l'introduction du vaccin conjugué et permis d'identifier des infections à *Haemophilus* dont le type était impossible à déterminer, associées à l'infection par le VIH.

## Resumen

### Repercusión de la introducción de la vacuna conjugada contra *Haemophilus influenzae* tipo b (Hib) en Sudáfrica

**Objetivo** Analizar las tendencias de los casos notificados de enfermedad invasiva por *Haemophilus influenzae* en Sudáfrica durante los cinco primeros años de utilización de la vacuna conjugada contra *Haemophilus influenzae* tipo b (anti-Hib) en el calendario de vacunación infantil sistemática.

**Métodos** Usamos los datos de vigilancia obtenidos por el laboratorio nacional para identificar los casos de enfermedad invasiva por *H. influenzae* registrados entre julio de 1999 y junio de 2004, así como las cepas aisladas enviadas para serotipificación y análisis de la sensibilidad a los antimicrobianos.

**Resultados** La cifra absoluta de casos de infección por Hib (notificados al sistema de vigilancia nacional) entre los niños menores de un año se redujo en un 65%, de 55 casos en 1999-2000 a 19 casos en 2003-2004. La vigilancia mejorada iniciada en 2003 identificó la infección por el virus de la inmunodeficiencia humana (VIH) y la vacunación incompleta como factores contribuyentes a la transmisión de Hib. El número total de casos de infección por *H. influenzae* confirmados en laboratorio se mantuvo inalterado debido a que la enfermedad de tipo no b se notificó con creciente frecuencia al sistema de vigilancia como consecuencia de la mejora del sistema. Los niños con enfermedad no tipificable tenían más probabilidades de ser VIH-positivos (32 de 34; 94%) que los niños con enfermedad por Hib (10 de 14; 71%), *P* = 0,051, y los aislados recientes de Hib tenían más probabilidades de ser multirresistentes (2% en 1999-2000, frente al 19% de 2003-2004, *P* = 0,001).

**Conclusiones** Los datos de un nuevo sistema nacional de vigilancia basado en el laboratorio mostraron una disminución de la carga de morbilidad por Hib entre los niños sudafricanos tras la introducción de vacunas conjugadas e identificaron casos de enfermedad no tipificable asociada a la infección por VIH.

## ملخص

### تأثير إنتاج اللقاح المقترن للنمط البائي للمستدميات النزلية في جنوب أفريقيا

**الهدف:** تحليل اتجاهات الأمراض الناجمة عن المستدميات النزلية التي أبلغ عن حدوثها في جنوب أفريقيا ضمن السنوات الخمس الأولى من إدخال اللقاح المقترن للنمط البائي للمستدميات النزلية ضمن الخطة الروتينية لتمنيع الأطفال.

**الطريقة:** استخدمنا معطيات الترصد المرتكز على المختبرات على الصعيد الوطني للتعرف على حالات الأمراض الناجمة عن المستدميات النزلية الغازية في الفترة بين تموز/يوليو 1999 وحزيران/يونيو 2004، وأجرينا تنميطاً مصلياً (اختبارات التعرف على الأنماط المصلية) واختبارات الاستجابة لمضادات المكروبات.

**الموجودات:** لقد نقص العدد المطلق للحالات الناجمة عن النمط البائي من المستدميات النزلية والتي أبلغ عنها في نظام الترصد الوطني بين الأطفال الذين تقل أعمارهم عن سنة واحدة من العمر بمقدار 65%، فبلغت 19 حالة في الفترة 2003 – 2004 بعد أن كانت 55 حالة في الفترة 1999 – 2000. وقد كشف الترصد المعزّز الذي أنشئ عام 2003 أن العدوى بفيروس الإيدز والتطعيم غير المستكمل هما من العوامل المساهمة في سراية النمط البائي من المستدميات النزلية. ولم يتغير الإبلاغ عن العدد الإجمالي من الحالات المؤكَّدة مختبرياً والناجمة عن المستدميات النزلية، نظراً لأن الإبلاغ عن الأمراض الناجمة عن الأنماط غير البائية من المستدمية النزلية في تزايد مستمر ضمن نظام الترصد، وذلك بسبب تعزيز هذا النظام. أما الأطفال الذين لم يكن بالإمكان التعرف على نمط المستدميات النزلية المسببة للمرض لديهم فلديهم احتمال أكبر لأن يكونوا إيجابيين لفيروس الإيدز، وبلغ عددهم 32 طفلاً من بين 34 طفلاً، وهذا يعادل 94%، وهذا أكبر من الاحتمال لدى الأطفال المصابين بالمرض الناجم عن النمط البائي من المستدميات النزلية (وبلغ عددهم 10 أطفال من بين 14 طفلاً، وهذا يعادل 61%، وقيمة احتمال 0.05). وقد كانت المستفردات الحديثة من النمط البائي من المستدميات النزلية أكثر احتمالاً لأن تكون مقاومة لأدوية متعددة، فقد كانت 2% في الفترة 1999 – 2000 وأصبحت 19% في الفترة 2003 – 2004، وقيمة احتمال 0.001.

**الاستنتاج:** تظهر المعطيات في نظام أنشئ حديثاً للترصد المرتكز على المختبرات على الصعيد الوطني تناقصاً في عبء الأمراض الناجمة عن النمط البائي من المستدميات النزلية بين الأطفال في جنوب أفريقيا تلو إدخال اللقاح المقترن والتعرف على الحالات الناجمة عن المستدميات التي لا يمكن التعرف على أنماطها والمرافقة للعدوى بفيروس الإيدز.

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