Epidemiology of Pertussis in a West African Community before and after Introduction of a Widespread Vaccination Program

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The control of pertussis remains a worldwide concern. Little has been documented about its epidemiology in Africa. The authors have studied pertussis in a prospective cohort of children in a rural West African community over a 13-year period comprising time before and after introduction of a vaccination program. Children under age 15 years who were residents of the Niakhar study area in Senegal were followed prospectively between January 1984 and December 1996 for the occurrence of pertussis. Morbidity and mortality rates were extremely high before the launch of immunization. Crude incidence was 183 per 1,000 child-years at risk under age 5 years, with a 2.8% case-fatality rate. After the introduction of the vaccination program, overall incidence dropped rapidly and dramatically—by 27% after 3 years and 46% after 6 years. The decline in incidence involved all age groups but was most substantial in the group under age 5 years and was particularly pronounced in unvaccinated infants. The median age of acquisition of the disease rose steadily with population vaccine coverage. This study shows the tremendous magnitude of the disease burden in children and the rapid decline after vaccination, and it suggests a strong herd-immunity effect.

Although pertussis is preventable by vaccination, it remains a ubiquitous, serious infectious disease, causing a worldwide estimated 40 million cases and 360,000 deaths each year, 90 percent of which occur in developing countries (1). As early as 1925, a vaccine was shown to be effective (2). It was the predecessor of the current whole-cell vaccines that have been in general use for nearly 50 years in industrialized countries, resulting in a drop in the incidence of pertussis to very low levels (1). However, despite good infant vaccine coverage, pertussis has recently appeared to be reemerging in these countries, featuring a modified epidemiology with a high incidence in early infancy and rising incidences in older children and adults (3–5).

The introduction of new acellular vaccines and the return of the disease in countries that have been vaccinating children for decades have reemphasized the need to evaluate the burden of pertussis in the developing world and to explore optimal control strategies (6). As part of the Expanded Programme on Immunization (EPI), whole-cell vaccines have been used widely in developing countries for decades. However, there is a lack of precise data to assess their actual effects on pertussis incidence and on age-specific morbidity in the population. Current efforts to improve routine immunization coverage as part of the Global Alliance for Vaccines and Immunization have also raised issues regarding pertussis disease burden (7).

This paper reviews the effects of a vaccination program with a high vaccine uptake on pertussis incidence and mortality in a rural Sahelian population of West Africa. We have studied a prospective cohort in the Niakhar study area in Senegal, where a long-term demographic and epidemiologic surveillance program was initiated in 1983 (8).

MATERIALS AND METHODS

Study setting

The Niakhar study area is located 150 km southeast of Dakar, Senegal, and comprises 30 villages. The community is composed of Sereer families who depend upon subsis-
tence farming (millet and sorghum), supplemented by cattle rearing and cultivation of groundnuts. Extended families reside in compounds. In January 1997, 29,104 residents were living in 1,838 compounds; 47 percent of these residents were under age 15 years. Mortality rates for infants and children under age 5 years were 7,900 and 18,500 per 100,000, respectively, in 1996.

Study population

Since March 1983, all residents have been under longitudinal observation based on annual or weekly (from 1987) visits to each compound. Trained, supervised field workers used structured questionnaires, and illnesses were checked through physician visits. This analysis was restricted to children under age 15 years who were residents of the area between January 1984 and December 1996. The study was conducted in accordance with the Helsinki Declaration of 1975 (revised 1983) (9).

Pertussis immunization

From 1980 to 1985, sporadic immunizations were performed mainly as single doses of diphtheria and tetanus toxoids—whole-cell pertussis vaccine—inactivated poliomyelitis vaccine (DTPwc-IPV; Tetracoq, Institut Mérieux (now, Aventis Pasteur), Lyon, France), reaching fewer than 5 percent of the children. From November 1986 to January 1987, Senegalese authorities conducted EPI mass immunization campaigns targeting children under age 5 years. From August 1987 onward, infants have been included in an immunization program based on monthly sessions, provided entirely by the research team as a local EPI mobile team, with rigorous record keeping. From 1987 to 1989, children received three doses of DTPwc-IPV at ages of approximately 3, 5, and 10 months, with repeated opportunities for transportation and callback. DTPwc-IPV was administered concomitantly with measles vaccines in the context of a clinical trial (10). From 1990 to 1996, children were immunized against pertussis at ages 2, 4, and 6 months as part of a clinical trial of the relative efficacy of an acellular vaccine (DTP-IPV; Tetravac, Aventis Pasteur, Lyon, France) versus a whole-cell vaccine (DTPwc-IPV (Tetracoq)) (11). Information on immunizations administered before 1987 was collected from parents and clinic records. Information on doses received outside the project was collected mainly from individual parent-held records. A child was considered to be fully immunized when he or she had received three doses of pertussis vaccine, without distinction between vaccines.

Pertussis surveillance and case definition

From 1984 to 1986, each compound was visited annually by a field worker. Information on immunizations and disease occurrence was collected from interviews with mothers and verified by surveys. From 1987 to 1996, each compound was visited weekly. From 1987 to late 1990, the trigger for notification of a suspected case of pertussis was “whooping cough,” as perceived by the mothers. Thereafter, the notification crite-
yielding a total of 6,180 episodes. In addition, 3.4 percent (204 of 6,060) of these children had histories of pertussis reported either on the initial census in 1983 (n = 67) or on immigration into the area (n = 137). Pertussis was endemic, with annual peaks and with epidemics every 3–4 years. Three epidemics were centered on 1986, 1990, and 1993 (figure 1). There has been a decrease both in the number of cases between epidemics and in the magnitude of the epidemic peaks. At the beginning of the period, there was a high level of endemicity of pertussis (an incidence of about 60 per 1,000 person-years in children under age 15 years in 1984–1985). From late 1987 (1 year after the launch of EPI) onward, there was a drop in the number of cases reported between epidemic years. A decrease in incidence was observed in every age group, more prominently among children under age 5 years. The latter, in whom the incidence had been highest initially, experienced a declining incidence that eventually reached the same incidence rate as the oldest age group. The greatest decline was achieved in children less than age 2 years. The declining trend was with a time lag according to the age group; it was more obvious in the early periods when the age of disease was lower (figure 2). The same observations applied when plotting the age per birth cohort (figure 3), where each line represents a longitudinal series of rates depicting the evolution of incidence within an age group.

If we consider the three epidemic years, an overall 25 percent decline in incidence was observed at each successive epidemic (table 1). The most spectacular decline was for the children aged 6–23 months, with a 79 percent total incidence reduction. However, the reduction was also obvious for infants under age 6 months, even for very young infants (<2 months), whose incidence dropped from 207.8 per 1,000 in 1986 to 56.4 per 1,000 person-years in 1993.

Age and gender distribution of cases

The median age of pertussis cases rose steadily from 4.1 years in 1986 to 5.3 years in 1990 and 6.2 years in 1993 (figure 2), with a comparable rise in nonepidemic years. Children less than age 5 years represented 60 percent of the cases in 1986, 48 percent in 1990, and 38 percent in 1993. This reduction was mainly due to a decrease in the number of children under age 2 years, who were 25 percent of the cases in 1986 but only 11 percent in 1993 (table 1). Annual incidences were always higher among girls (table 1), with an overall gender ratio of 1.1 (95 percent confidence interval: 1.0, 1.1) for the period.

Mortality and case-fatality rate

The greatest mortality was observed for children under age 5 years, among whom pertussis represented 9 percent of the causes of death in 1986, affecting mainly children under

age 2 years (table 2). In 1990, mortality declined, with no deaths in children above age 2 years, but the mortality rate remained high (9.0 per 1,000 person-years) for infants less than age 6 months, dropping to 1.7 per 1,000 person-years in 1993. The same observations also applied for the case-fatality rates. Rates were higher in girls.

FIGURE 3. Age-specific incidence rates of pertussis per cohort, Niakhar, Senegal, 1984–1996. As an example, the first point of the “<5 years” line in 1984 represents the incidence for children born in 1984 during the period when they were under age 5 years. Incomplete lines are due to the restriction of the observation period to 1984–1996 and to the age grouping of the data for improved readability. For example, in the younger group (<2 years), the first complete information was available for the cohort born in 1984 and the last for the cohort born in 1994.
are derived from active, population-based surveillance, the highly vaccinated population (1, 18–21). Because our results suggested by our data as well as by recent analysis of data a substantial effect of vaccination on pertussis transmission is more effective in preventing disease than transmission (16). A consistent periodicity, it has been suggested that the vaccine is (Simondon et al., unpublished data)). On the basis of this consistent periodicity, it has been suggested that the vaccine is more effective in preventing disease than transmission (16). A substantial effect of vaccination on pertussis transmission is suggested by our data as well as by recent analysis of data from the United Kingdom (15, 17).

The notification efficiency of pertussis is notoriously poor, and the disease is often underdiagnosed, particularly in a highly vaccinated population (1, 18–21). Because our results are derived from active, population-based surveillance, the incidence rates found here are higher than those passively reported in prevaccine Europe and North America (98–1,000 cases per 100,000 inhabitants) or by most developing countries (10–100 per 100,000 inhabitants 1974 to 1990), even in Africa (up to 1,000 per 100,000) (22). The observed incidence is similar to that in a population-based study conducted in the 1970s in Machakos, rural Kenya, (1,600 per 100,000 children under age 15 years) (23).

In the conditions of this study (high pertussis incidence, substantially unvaccinated population, and diagnosis by a seasoned physician without knowledge of vaccination history), the clinical diagnosis of pertussis by a physician has been found to be a highly reliable diagnostic method (24). In the first 4 years of the study, we used only the mothers’ diagnosis. Although this may have resulted in a potential undercount of cases, the declining incidence observed over time occurred in the face of an increased sensitivity in the case definition, moving from a mother’s to a physician’s diagnosis with expanded notification criteria.

Few children developed more than one episode of pertussis (21, 25). The initial case-fatality rate of 1.71 percent decreased to 0.11 percent, which is close to rates reported from industrialized countries (0.04 percent on average) (22). Morbidity and mortality were slightly higher for girls (23, 25, 26). The median age at acquisition of the disease before the vaccination program was 4.1 years, close to that found in England (4.4

### DISCUSSION

These data quantify the tremendous magnitude of the pertussis burden in a developing country before the recent introduction of vaccination. The disease was present in every season, causing huge epidemics with a high case-fatality rate. The introduction of pertussis vaccine through the EPI resulted in a rapid and substantial decrease in incidence, particularly in infants under age 6 months. This might suggest that even a single dose imparted some protection, but also reflects a high level of vaccine-induced herd immunity, given the reduction in incidence in unvaccinated infants under age 2 months, as reported in the United Kingdom (15). High levels of vaccine coverage appear to have dampened the annual cycles while not obviously affecting the longer-term fluctuation (3- to 4-year periods). (A subsequent epidemic occurred in 1997, (Simondon et al., unpublished data)). On the basis of this consistent periodicity, it has been suggested that the vaccine is more effective in preventing disease than transmission (16). A substantial effect of vaccination on pertussis transmission is suggested by our data as well as by recent analysis of data from the United Kingdom (15, 17).

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### TABLE 1. Pertussis case distribution and incidence per age and sex, during epidemic years, Niakhar, Senegal, 1984–1996

<table>
<thead>
<tr>
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<tbody>
<tr>
<td></td>
<td>Cases</td>
<td>No. of PYR</td>
<td>Incidence per 1,000 PYR</td>
</tr>
<tr>
<td>0–5 months</td>
<td>97</td>
<td>1,443</td>
<td>155.2</td>
</tr>
<tr>
<td>6–23 months</td>
<td>246</td>
<td>5,643</td>
<td>88.0</td>
</tr>
<tr>
<td>2–4 years</td>
<td>492</td>
<td>2,530</td>
<td>98.5</td>
</tr>
<tr>
<td>5–14 years</td>
<td>570</td>
<td>6,481</td>
<td>88.0</td>
</tr>
<tr>
<td>Total (0–14 years)</td>
<td>1,405</td>
<td>11,036</td>
<td>127.3</td>
</tr>
<tr>
<td>Girls</td>
<td>721</td>
<td>5,395</td>
<td>133.6</td>
</tr>
<tr>
<td>Boys</td>
<td>684</td>
<td>5,641</td>
<td>121.3</td>
</tr>
<tr>
<td>RR† (95% Cl)</td>
<td>1.1 (1.0, 1.2)</td>
<td>1.0 (0.9, 1.2)</td>
<td>1.1 (1.0, 1.3)</td>
</tr>
</tbody>
</table>

* PYR, person-years at risk; RR, relative risk (girls/boys); Cl, confidence interval.

### TABLE 2. Pertussis proportion among all deaths and mortality and case-fatality rates per age and sex during the first two epidemic years, Niakhar, Senegal, 1984–1996

<table>
<thead>
<tr>
<th>Age</th>
<th>First outbreak (1986)</th>
<th>Second outbreak (1990)</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>No. of pertussis deaths</td>
<td>Proportion among deaths (%)</td>
</tr>
<tr>
<td>0–5 months</td>
<td>4</td>
<td>4.3</td>
</tr>
<tr>
<td>6–23 months</td>
<td>9</td>
<td>9.2</td>
</tr>
<tr>
<td>2–4 years</td>
<td>10</td>
<td>12.7</td>
</tr>
<tr>
<td>5–14 years</td>
<td>1</td>
<td>4.0</td>
</tr>
<tr>
<td>Total (0–14 years)</td>
<td>24</td>
<td>8.1</td>
</tr>
<tr>
<td>Girls</td>
<td>13</td>
<td>8.8</td>
</tr>
<tr>
<td>Boys</td>
<td>11</td>
<td>7.4</td>
</tr>
</tbody>
</table>

* Only one death was observed during 1993, the last epidemic year (syncopal apnea in a 2-month-old girl).

† PYR, person-years at risk.
years) and in Massachusetts in 1945 (5.2 years) (26) or in rural Kenya in the 1970s (3.5 years) (23). Although Morley et al. (26) described a lower median age in developing countries (1.4–3.1 years), such clinic-based studies with bias to selection of disease of higher severity are therefore at younger ages. We observed an upward shift in the age distribution of cases when vaccine coverage improved, as reported elsewhere (27–29).

The dramatic decline in disease incidence in this population is the ultimate goal of a vaccination program. However, the low incidence might be a transition “honeymoon period” to a new epidemiologic equilibrium, as observed and predicted for measles (28, 30). The return of substantial occurrence of the disease in this context could have much more impact than that recently seen in the United States and in Europe (31) because of a lack of booster doses. In addition, a progressively increasing proportion of infants will be born to mothers who are immune due to vaccination in early childhood as opposed to being immune due to natural exposure. Further understanding of the effects of vaccines on susceptibility to and infectiousness of pertussis and how this may alter the relation between age and disease, as well as prolonged epidemiologic studies, are warranted.

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REFERENCES