Invited Commentary: Pertussis, A Forgotten Killer

Philippe Duclos and Jean-Marc Olivé

Pertussis remains one of the major causes of childhood morbidity and mortality at the global level. Widespread immunization coverage with diphtheria-tetanus-pertussis (DTP) vaccines is the cornerstone of prevention. However, with the lack of a specific global disease reduction target and although coverage with three doses of DTP vaccine is a major indicator of immunization programs (1), pertussis has not received sufficient emphasis in recent years. This is despite the annual global occurrence of millions of cases, with an estimated 296,000 remaining deaths (2), and the wide availability of effective vaccines (3). Yet pertussis surveillance is difficult, and disease burden due to this pertussis goes largely unrecognized. To raise the profile of pertussis, more effective surveillance tools are needed, particularly in developing countries, if the disease is to come under control.

A meeting on pertussis surveillance was organized on October 16–18, 2000, under the aegis of the World Health Organization (WHO) (4) to focus on surveillance as a fundamental support for control strategies. It highlighted that pertussis surveillance was carried out in some countries, but was not done in any meaningful sense in three quarters of the world. Surveillance data and coverage data are both unreliable and yet are needed to monitor immunization programs. The meeting highlighted the fact that the lack of use of standard definitions, guidelines, and laboratory confirmation hindered pertussis surveillance and resulted in a series of recommendations and modified case definitions and surveillance standards for pertussis. It called for outbreaks to be investigated promptly to determine their cause and to ensure proper case management and for sentinel surveillance sites to be developed in a few major hospitals. The meeting also emphasized that the quality of DTP coverage data should be improved and monitored by dose and that countries should be encouraged to record administration of booster doses. It stressed the need for laboratory standardization and for WHO to develop laboratory guidelines. Meeting participants also insisted that better data on disease burden in developing countries were urgently needed to validate estimates of global disease burden. Work was indeed started to revise and improve the method for estimation of global pertussis burden. This method is being further refined and validated with an attempt to include the impact of partial vaccination and of timeliness of vaccination (4).

In that context, one should applaud the publication of the work by Préziosi et al. (5) on the epidemiology of whooping cough in a West African community before and after introduction of a widespread vaccination program. Yet one must keep in mind that the study covers only a small fraction of the Senegalese population and suffers from some methodological limitations such as the use of variable and not very specific case definitions and differences in follow-up over the study period, the lack of laboratory confirmation, and the fact that this is essentially presented as an ecologic study. The specific routine immunization schedule of 3, 5, and 10 months and then 2, 4, and 6 months and the implementation of a mass vaccination campaign for children under age 5 years from November 1986 to January 1987 must be kept in mind prior to extrapolating, lest one overinterpret conclusions from the paper by Préziosi et al. In addition, the fact that all pertussis vaccines are not necessarily equivalent in terms of efficacy should be taken into consideration prior to generalization of the results. One must, however, also highlight the fact that there are very few studies of the epidemiology of pertussis and the impact of pertussis immunization programs in developing countries (6) and that this study enjoys a fairly thorough follow-up and documentation of the immunization status.

Four specific points are raised by the authors and deserve to be highlighted and discussed further. First, Préziosi et al. (5) clearly point out the tremendous burden of the disease and the impact of the pertussis immunization program both in terms of morbidity and of mortality reduction. If we were to extrapolate from their data to the entire current Senegalese population, nearly 8,000 children under age 5 years would die each year from pertussis-related death in the absence of the immunization program. Considering that, based on current coverage, an estimated 1,500 deaths would continue to occur every year in Senegal. Thus, it can be estimated that nearly 6,500 deaths are prevented every year, on average. It must be noted, however, that at country level the increase in coverage over the study period may not have been so dramatic since, according to data reported to WHO and the United Nations Children’s Fund (Anthony Burton, Department of Vaccines and Biologicals, WHO, personal communication, 2002), coverage was estimated to have increased from 35 percent in the early 1980s to only approximately 60 percent in
1999, although true coverage might be higher because of catch-up after age 1 year.

Second, not only was mortality reduced from accounting for 9 percent of all deaths in 1986 but the overall case fatality rate was also decreased from 1.71 to 0.11 percent. This might reflect either the occurrence of a larger proportion of cases in older groups (and, therefore, less severe cases) or better case management. At least throughout the 1990 outbreak, the case-fatality rate remained substantially high, that is, 7 percent in children less than age 6 months as well as in children aged 6–23 months. This suggests that the overall reduction in the case-fatality rate is due to the former of the two proposed explanations.

Third, the presented numbers emphasize the big difference between children who received at least one dose of vaccine (41.7 percent) and those who completed the series (28.9 percent) over the entire study period. Although one dose offers little protection against disease, it might offer significant protection against death. The actual effect of such a single dose is still largely undocumented, and the authors may have sufficient information in their database to support or invalidate such a hypothesis. This would be worth exploiting further.

Fourth, the authors make the point that their study suggests a strong herd-immunity effect. Although the reduction of incidence from 207.8 per 1,000 in 1986 to 56.4 per 1,000 in 1993 for infants less than age 2 months (i.e., a reduction by 73 percent in the assumed absence of vaccination at this young age) would seem to support such an effect, this is hard to reconcile with the more limited effect in the older groups. In the age group 5–14 years, the reported reduction in incidence of only 19.3 percent between the two outbreaks could be accounted for almost entirely by the increase in coverage of 15–20 percent in this group according to figure 1 in the article by Préziosi et al. (5). Similarly, in the age group 2–4 years, the 58 percent decrease was lower than the 70 percent increase in coverage. Also difficult to understand is the relatively limited decrease in incidence (60 percent) in the age group 0–5 months (compared with that in children less than age 2 months and therefore unvaccinated) when a substantial proportion of children in this extended group would have received some vaccination. Disease exposure should not be substantially different from that in the infants aged less than 2 months. The largest decrease was observed in children aged 6–23 months—a 79 percent reduction. Although one might argue that vaccine failures should be taken into consideration and that herd-immunity effect might be stronger than it seems, the authors provide no such information (although it might be available to them). The article falls short of making a strong case for a large herd-immunity effect and on that point adds little to previously published work (7–11). Pertussis can occur in previously immunized and infected persons, but immunization and prior infection attenuate the clinical course of the disease. It is also accepted that pertussis vaccination does prevent infection and has some limited herd-immunity effect. The paper by Préziosi et al. provides no evidence that reaching a certain level of coverage would stop circulation through herd immunity. On the contrary, at least in the older groups, it is compatible with the hypothesis used in the modeling of revised burden estimate, that is, that vaccination does not significantly affect transmission in the unvaccinated (4). Since vaccination status seems to have been available to the authors, further analysis of age-specific pertussis incidence depending on individual vaccination status might shed further light on herd immunity, which may vary depending on vaccine used.

The paper by Préziosi et al. provides also an opportunity to remember that the WHO Expanded Programme on Immunization recommends that pertussis vaccination be given at an early age (i.e., 6, 10, and 14 weeks), with the aim of maximizing impact on the prevention of severe complications and deaths from pertussis, which occur at a very young age, as evidenced by their findings. It remains important to start immunization at as early an age as possible, particularly in countries where coverage is limited and case-fatality rates remain substantially high.

The authors should be praised for making a useful contribution. It is hoped that this will encourage publication of more studies of pertussis burden/epidemiology. The authors should also be encouraged to continue monitoring and reporting on the impact of the pertussis vaccination program in the Niakhar cohort in order to better understand the long-term impact of the program.

**REFERENCES**