Infant Pertussis: What to Do Next?

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(See the Major Article by Skowronski et al, on pages 318–27.)

The resurgence of pertussis during the past 30 years, despite record high immunization rates in infants and children, has led some to label pertussis as the most poorly controlled vaccine-preventable disease in the developed world. The high incidence of pertussis disease in infants too young to be immunized, resulting in substantial morbidity and mortality, is the driving force behind recent prevention strategies [1, 2]. As many as 75% of pertussis-infected infants acquire the disease from a household contact, most often a parent [3–7]. The need for effective preventive strategies was emphasized during the widespread 2010 pertussis outbreak in California. More persons were affected than had been in any single year during the prior 6 decades; the outbreak resulted in an infection rate of 435 cases per 100,000 population in infants <6 months old and 10 infant deaths, all <3 months of age [8]. Unfortunately, young infants have accounted for >90% of pertussis-related deaths in the United States in the 21st century.

The Advisory Committee on Immunization Practice (ACIP) of the Centers for Disease Control and Prevention addressed this public health issue in 2006 by recommending cocooning of infants [9]. Cocooning is the targeted immunization of postpartum women and all contacts of their infants during the first year of life, preferably before their birth or hospital discharge. It had been estimated that, when perfectly implemented, cocooning could potentially reduce pertussis cases in infants <3 months old by 70% [1]. The ACIP recommendation was based on similar proposals in other countries and concurred with the Global Pertussis Initiative view that, notwithstanding the absence of outcome and cost-effectiveness data, cocooning was worth pursuing because “even protecting just some infants would be considered a success” [1].

Implementation of cocooning has been challenging. Logistic and reimbursement issues have hampered hospital and healthcare organizations from immunizing postpartum women with tetanus and reduced diphtheria toxoids and acellular pertussis (Tdap) vaccine. Reports from the few programs implementing Tdap for postpartum women indicate that such programs require an intense focus on parental education and must either have longer than usual windows of opportunity to administer Tdap to parents (eg, when infants are admitted to neonatal intensive care units), or innovative strategies with dedicated funding sources and provide vaccine without reimbursement [10–13]. Financial constraints are major barriers to successful cocooning.

In this issue of the Journal, Skowronski et al [14] provide one of the first cost-effectiveness evaluations of a parental cocooning strategy applied to 2 Canadian provinces, Quebec and British Columbia, both currently experiencing record low rates of pertussis. By use of province-specific pertussis surveillance trends from 1990 to 2010 and contemporary infant pertussis illness rates, hospitalization data, and mortality data, coupled with infant illness rates attributable to parent exposure and vaccine-effectiveness rates from the literature, they report that immunization of new parents with Tdap (ie, partial cocooning) is expensive and resource intensive in areas where pertussis incidence is low. The number needed to vaccinate exceeds 10,000 to prevent 1 infant hospitalization, ~100,000 to prevent 1 infant intensive care admission, and >1 million to prevent 1 infant death. This epidemiologic construct contradicts more optimistic outcome estimates but provides useful data for financially strapped public health agencies. The findings of Skowronski et al [14] are not necessarily applicable to areas experiencing high rates of endemic pertussis.
disease or pertussis outbreaks or to communities with large concentrations of Hispanic infants, who are known to have high rates of pertussis when compared with other ethnicities in the United States [15]. It is possible that immunizing new parents contributes substantially to pertussis herd immunity and would affect a further adjustment of the cost of such an initiative. Ultimately, the cost of programs must be balanced against the costs of providing prolonged intensive care with mechanical ventilation or extracorporeal membrane oxygenation for some infants, as well as the incalculable cost of infant death.

The fact remains that even if cost-effectiveness analyses were favorable for cocooning to prevent infant pertussis, it is a labor-intensive and logistically difficult initiative to implement. To our knowledge, no programs to date have successfully implemented Tdap vaccination of fathers or other contacts before the birth of the infant, although this is most desirable from a biological standpoint. Cocooning is inherently limited in its ability to prevent infant pertussis in the first few weeks of life because pertussis may be circulating in a household at the time of birth, or may be introduced before sufficient time has elapsed for an immune response among Tdap-vaccinated contacts [13, 16].

What are the options to prevent life-threatening pertussis in very young infants if even partial cocooning is too difficult or too expensive? Neonatal acellular pertussis immunization has been studied, with mixed reports. Administration of a 3-component pertussis vaccine showed a promising and earlier immune response when either a single [17–19] or 2-dose schedule at 0 and 1 months of age [20] was used in combination with diphtheria-tetanus toxoids and acellular pertussis (DTaP) vaccine at either 2, 4, and 6 months or 3, 5, and 11 months of age. Administering DTaP vaccine in the first 2 weeks of life did not improve the pertussis immune response [21]. Interference with antibody responses to other recommended vaccines of varying degrees was noted in all but one study and sometimes persisted into the second year of life [18–20]. Thus, although neonatal immunization is worthy of further investigation, the facts to date appear to limit this approach.

Maternal immunization mimics nature’s gift of passive immunity to the newborn infant. Theoretically, achieving high maternal pertussis-specific immunoglobulin G would passively protect the infant for the first few months of life. Anecdotal data from the prevaccine period appear to support this concept [22]. Maternal immunization with whole-cell pertussis vaccine late in pregnancy was reported to be safe for mothers and infants and resulted in high levels of pertussis-specific antibodies in infants. Contemporary studies confirm that active placental transfer of naturally acquired and vaccine-induced pertussis-specific antibodies occurs, and durability of such passively acquired antibody has been demonstrated [23–28]. Despite concerns that high concentrations of maternal antibodies could interfere with the infant’s immune response to active immunization with DTaP vaccine, data suggest that naturally acquired maternal pertussis-specific antibodies do not significantly interfere with an infant’s immune response to active immunization with acellular pertussis vaccines [29]. Although phase 1 maternal Tdap immunization studies are ongoing, these combined data suggest that Tdap immunization in late pregnancy should induce concentrations of maternal pertussis-specific antibodies in the infant that are high enough to protect against pertussis through the period of highest risk, and may be more cost-effective than cocooning. In June 2011, ACIP recommended Tdap immunization in the third or late in the second trimester of pregnancy in preference to cocooning, to prevent pertussis-related mortality in young infants [30]. It was noted that this strategy should be combined with efforts to cocoon the infant by immunizing as many infant contacts as possible, because passively acquired maternal antibodies to pertussis were unlikely to persist in protective concentrations beyond 3 months of age. Furthermore, maternal immunization would probably have little impact on disease rates in preterm infants in whom the risk of mortality is high [5]. There are no proven safety concerns regarding Tdap administration in pregnancy, but it is likely that, as with influenza vaccine, this immunization recommendation will take some years to be implemented fully.

Skowronski et al [14] have demonstrated aptly the challenges in justifying cocooning as a stand-alone strategy to prevent infant pertussis in areas of low pertussis prevalence [14]. It is likely that, as with other infectious diseases, no single paradigm will effectively control pertussis in infants. Nevertheless it seems logical that every effort to protect young infants through maternal immunization and indirectly through cocooning to prevent later exposures and improve herd immunity should be undertaken so that the elimination of fatal infant pertussis becomes a reality.

Note

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