How Can We Best Prevent Pertussis in Infants?

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(See the article by Castagnini et al, on pages 78–84.)

Pertussis is a very contagious respiratory infection, and despite a high rate of vaccine coverage, it is the only vaccine-preventable disease currently increasing in the United States. In 2009 a total of 16,858 cases of pertussis with 12 infant deaths were reported by the Centers for Disease Control and Prevention [1], and 10 infant deaths were also documented in a recent outbreak of pertussis in California [2, 3]. Because infants represent the most severely affected age group, particularly infants <2 months of age who are too young to have received vaccine, innovative immunization strategies are needed to protect this vulnerable population.

Several strategies, including vaccination of newborns, older adolescents and adults, and pregnant women, have been proposed to decrease the rate of pertussis in very young children. One of these strategies, the “cocoon strategy,” seeks to protect newborn infants from subsequent pertussis exposure by administering tetanus and diphtheria toxoids and acellular pertussis (Tdap) vaccine to mothers and other close household contacts before postpartum hospital discharge. Earlier reports demonstrated that nearly 75% of pertussis cases in young infants resulted from exposure to an asymptomatic or mildly symptomatic household member, with the mother identified as the source of the infection in 33% of the cases [4, 5].

Thus, it was postulated that cocooning could protect the infant from household contagion in up to 75% of cases.

Computer simulations were used to test the potential impact of 6 immunization strategies on the burden of pertussis in young infants [6]. These strategies included (1) routine childhood diphtheria and tetanus toxoids and acellular pertussis (DTaP) vaccinations at 2, 4, and 6 months of age, with boosters at 12–15 months and 4–6 years of age; (2) routine childhood DTaP vaccinations and routine Tdap immunization of adolescents at 12 years of age; (3) routine childhood DTaP and routine Tdap immunization of adolescents and adults at 10-year intervals; (4) routine childhood DTaP and cocooning of infants by immunization of household contacts; (5) routine childhood DTaP vaccinations, routine Tdap immunization of adolescents at 12 years of age, and cocooning; and (6) routine childhood DTaP, routine Tdap immunization of adolescents and adults at 10-year intervals, and cocooning. The simulations showed that the incidence of typical pertussis in young children (0–23 months of age) decreased with all 5 new strategies, but significant reductions in disease rates in very young children (<3 months of age) were projected only with the cocoon strategy. On the basis of these simulations and the need for disease prevention in the youngest children, the Centers for Disease Control and Prevention recommended universal “cocooning” in 2006 [7].

In this issue of the journal, Castagnini and colleagues [8] studied the impact of maternal postpartum Tdap immunization, “cocooning,” on infant pertussis infection. The cocooning intervention took place at 1 hospital, the Ben Taub General Hospital (BTGH) in Houston, Texas, with a predominantly Hispanic, largely medically underserved population. An active educational effort at BTGH informed the pregnant women about the program and provided vaccine at no charge to the patient. During the intervention period, 67% of postpartum women at BTGH received Tdap vaccine. Most women not receiving vaccine had been recently immunized with tetanus-containing vaccines or had contraindications to vaccination.

To measure the impact of the cocooning strategy, the authors conducted a cross-sectional study in 4 Houston hospitals and evaluated the number of laboratory-confirmed pertussis cases in children <6 months of age before (July 2000 through December 2007) and after the cocooning strategy (January 2008 through May 2009). Cases of pertussis
were identified from the 4 participating sites, including BTGH, by International Classification of Diseases, Ninth Revision (ICD-9) codes reporting pertussis or whooping cough as primary or secondary diagnoses coupled with laboratory-confirmed pertussis (positive bacterial culture, direct fluorescence, or polymerase chain reaction [PCR]). A total of 514 infants with laboratory-confirmed infection were included in the study, 378 from the preintervention and 136 from the postintervention period, with identical proportions of infants with laboratory-confirmed pertussis born at BTGH during the 2 study periods.

Does this study indicate that cocooning should be abandoned? Why was there no measurable impact on pertussis disease? Several possible explanations exist. One possibility was that a strategy directed only at postpartum mothers would not reduce the other sources of contagion in the household and that for cocooning to be successful, all the household contacts would need to be immunized in the postpartum period. However, administering vaccine in the hospital setting to all household contacts who are not hospitalized themselves would pose major logistic difficulties. Another possible explanation for the lack of impact on pertussis was that not enough women were immunized to actually test the intervention. Postpartum immunization only occurred at 1 hospital and probably did not have sufficient impact on pertussis disease in the entire community because <10% of the children in the study population were born at BTGH in both the pre- and postintervention periods. If the cocooning strategy had been employed at all 4 study hospitals, then perhaps the impact would have been greater, but so would have been the costs and the logistic difficulties. An additional possibility was that the vaccine was given too late, because the induction of antibody to pertussis generally takes ~2 weeks [9]. If the mother were already exposed or infected, postpartum vaccination would be too late to protect the mother and likely too late to protect the infant. Another complexity of the study was the use of the sensitive diagnostic method PCR during the postintervention and not the preintervention period, potentially identifying more cases in the postintervention period. However, it is unlikely that PCR would have differed between infants born to immunized and those born to unimmunized mothers. Finally, pre- and postintervention time periods differed in duration (7 vs 2 years, respectively), and the 3–4-year cyclic nature of pertussis circulation could have influenced pertussis rates in the pre- and postintervention periods.

Although this report did not support the effectiveness of the cocooning strategy for the reduction of pertussis infection in the study population, it should be interpreted cautiously, because the study had several limitations and may have underestimated the impact of the intervention. However, the cost and logistic barriers to widespread implementation of cocooning are major limitations and argue that cocooning is not the best overall approach to reduce the burden of pertussis in the youngest children.

The Advisory Committee for Immunization Practices recently recommended that Tdap vaccine be administered to all pregnant women [10] to provide protection for both the mother and her newborn infant during the earliest months of life. We and others have shown effective transplacental transmission of maternal antibodies [11, 12]. These antibodies should protect the infant against pertussis during the first months of life, when the infection can be very severe and before DTaP vaccine is routinely given. Although concern exists regarding the interference of maternally derived antibodies with the child’s immune response to the recommended infant DTaP vaccination, we are hopeful that the benefits will outweigh the theoretical concerns.

Previously Van Savage et al [13] and Englund et al [14] showed that infant immune responses to acellular pertussis vaccines (DTaP) were not affected by preexisting antibodies against pertussis toxin, although interference was noted in recipients of the conventional whole-cell pertussis vaccine (DTP). Studies of pertussis vaccination of pregnant women are ongoing and should soon provide an estimate of the impact of maternal antibody on immune responses to DTaP administered at 2, 4, and 6 months of age. In the meantime, the immunization of pregnant women with Tdap should be implemented to reduce infant mortality due to this serious disease. This will be a lofty goal, because immunization rates in pregnant women have lagged behind what is universally recommended for many vaccines, including influenza. Finally, efforts to immunize all members of the population are important, in addition to immunizing pregnant women. Only with extended pertussis immunization of children, adolescents, and adults will this highly contagious disease be controlled.

**Note**

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**References**

