Reply to Leuridan et al

We thank Leuridan and colleagues [1] for their helpful contribution to the deliberation on strategies to prevent life-threatening pertussis in very young infants.

It is not surprising that, in the absence of “boosting” through natural infection, tetanus, diphtheria, and acellular pertussis (Tdap) immunization of women preconception results in higher pertussis-specific immunoglobulin G (IgG) in subsequent infants at birth than in unimmunized women. Leuridan et al [1, 2] demonstrated this in their cohort of women immunized with Tdap between 2 sibling pregnancies. As Leuridan and colleagues indicate, our study lacked a control group [3]; however, the geometric mean concentration (GMC) of pertussis-specific IgG in cord blood was 1.8- to 2-fold higher than a similar cohort at our study site shortly before Tdap licensure [4]. Similar to Leuridan et al’s observations, the majority of infants born to Tdap-immunized mothers in our cohort had PT-specific IgG serum concentrations of >5 ELISA units (EU)/mL (87%) compared to 62% in sera of women from the same hospital during the prevaccine era (authors’ unpublished data). This is to be expected given the short median interval between vaccination and delivery in both their and our studies. However, for infant protection through age 2 or 3 months, when the primary immunization series starts depending on the country of birth, having merely a detectable PT-specific IgG at birth is unlikely to be protective. Maternally derived, PT-specific IgG antibody decays quickly; the estimated half-life from the pre-Tdap era is 36 days [5] and may be shorter following Tdap, as observed by Leuridan et al [1]. Because infants depend solely on antibody and lack the ability to mount cell-mediated responses when infected, an anti-PT of 5 EU/mL is unlikely to protect them through the period of highest risk for mortality and morbidity. Even if this modest level is sufficient, a policy of preconception Tdap means that 41% of infants may be vulnerable [3].

We agree that future studies should examine antibody kinetics when Tdap is administered late in pregnancy, as currently recommended in some countries [6–8]. Our cohort had only 3 women fulfilling these criteria, of whom 1 was immunized before the recommended optimal window [6–8] and 1 did not mount a robust immune response, thus limiting our ability to draw any meaningful conclusions. It was noteworthy that placental transfer was higher in women immunized during pregnancy than preconception [3]. Future research should better define the durability of acellular pertussis–induced immune responses in pregnant and nonpregnant individuals, the optimal timing of maternal immunization for optimal infant protection, the variability of antibody kinetics between different populations, the impact of such strategies on infant immune response to their primary immunization series, and, ultimately, the impact on infant infection. Such data are urgently needed to inform public policy. It is likely that in the absence of more-effective pertussis vaccines, no single strategy will suffice and, as with other infections, a multifaceted response is required to decrease pertussis-related morbidity and mortality in young infants.

Note

Potential conflicts of interest. C. M. H. is the recipient of research grants from Sanoﬁ Pasteur and Novartis Vaccines and Diagnostics, and serves on an advisory board for Novartis Vaccines and Diagnostics. C. J. B. is a consultant for Novartis Vaccines and Diagnostics. M. A. R. reports no potential conflicts.

All authors have submitted the ICMJE Form for Disclosure of Potential Conﬂicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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References


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