Impact of Vaccination During Pregnancy on Infant Pertussis Disease

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Pertussis vaccination during pregnancy has been implemented in many high-resource countries. Recent data from the United States, the United Kingdom, and South America demonstrate its effectiveness in reducing infant pertussis in the first 2 months of life.[1–3] However, suppression or "blunting" of the infant's subsequent response to primary immunization by maternally derived antibody has been demonstrated for many antigens.[4–6] Voysey et al compiled data on 7630 infants from 32 studies in 17 countries and demonstrated that preexisting maternally derived antibody inhibited infant antibody responses to priming doses for 20 of 21 vaccine antigens evaluated, including pertussis, with antibody responses for some antigens suppressed for periods up to 24 months.[7] Other reports have documented that tetanus toxoid and reduced diphtheria toxoid and acellular pertussis vaccine (Tdap) administration to pregnant persons suppresses primary infant antibody responses to pertussis, diphtheria, and pneumococcal conjugate vaccines.[4–6] What has not been well established, however, is whether this blunting has clinical consequences. Is early infant disease reduced at the expense of higher incidence at older ages? The recent report by Regan et al from Australia in this issue of *Pediatrics* addresses this important question.[8]

Tdap vaccination programs during pregnancy were initially established in Australia between 2014 and 2015 and federally supported in all jurisdictions by 2018.[9] Using administrative health records from 3 Australian regions, the authors conducted a population-based cohort study of 279 418 mother–infant pairs. Tdap receipt by pregnant persons was verified ≥14 days before delivery and pertussis infection was documented by review of notifiable disease records from these 3 regions, with most pertussis cases confirmed by polymerase chain reaction. Primary immunization records were available from the 2 largest regions, but not the third, to document infant receipt of 3 diphtheria and tetanus toxoids and acellular pertussis vaccines.

Maternal Tdap vaccine effectiveness (VE) and its impact on VE of the primary diphtheria and tetanus toxoids and acellular pertussis series in infants was determined. Overall, Tdap was administered to half of the pregnant persons in these 3 regions, generally at 28 to 31 weeks of gestation. The VE of maternal Tdap vaccination among infants <2 months old was 70.4% (95% confidence interval, 50.5%–82.3%), with no impact of gestational age at vaccine receipt on VE. However, among infants 7 to 8 months of age, VE for maternal Tdap declined to 43.3% (95% confidence interval, 6.8%–65.6%) and by 8 months of age, maternal Tdap was no longer effective.[8] In addition, VE point estimates for the third dose of infant pertussis vaccine among infants whose mothers received Tdap during pregnancy were lower when compared with infants of unvaccinated mothers (76.5% vs 92.9%, $P = .0024$), supporting the impact of blunting by maternal Tdap receipt. During the first 18 months of age, a total of 331 pertussis cases were identified in the cohort; 119 cases were identified among infants of vaccinated mothers, whereas 212 cases were identified among infants of unvaccinated mothers. Thus, the consequences of Tdap administration to pregnant persons was a reduction in early onset cases and overall, fewer cases with maternal immunization within the

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first 18 months of life. Furthermore, because pertussis disease is most serious in the first few months of life and fatalities are nearly always seen in this age group, protection against early disease before the onset of primary immunization in infants is critical.[10] Although pertussis disease globally was reduced during the SARS-CoV-2 pandemic, a recent report from New Zealand of 2 infant pertussis deaths support continued vigilance.[11]

Similar data were recently reported from the US Centers for Disease Control and Prevention, where an ecologic study of infant pertussis cases reported through the National Notifiable Diseases Surveillance System between January 1, 2000, and December 31, 2019, were analyzed.[12] Pertussis incidence rates were compared between the prematernal Tdap vaccination period (2000–2010) and the postmaternal Tdap vaccination period (2012–2019). During the prematernal Tdap vaccination period, annual pertussis incidence did not change among infants younger than 2 months and increased slightly among infants aged 6 months to <12 months. However, during the postmaternal Tdap vaccination period (2012–2019), pertussis incidence significantly decreased among infants younger than 2 months and remained unchanged among infants aged 6 to 12 months. As with the Australian data, the US data support the overall benefit of the maternal Tdap program and as with the Australian data do not suggest that blunting has led to an increase in cases within the first year of life.

Despite these encouraging data demonstrating the important role of maternal immunization in reducing pertussis disease, Tdap immunization rates during pregnancy in Australia, the United Kingdom, and the United States remain between 50% and 60%[13,14]; active engagement to increase these rates should be implemented. In addition, the promising studies of the efficacy of maternal immunization against respiratory syncytial virus and group B streptococcal disease on disease burden suggest that maternal immunization for these additional pathogens might soon be implemented. The consequences of maternally derived antibody on infant responses will need to continue to be monitored, as was done in the carefully conducted study of pertussis reported in this issue of *Pediatrics*. It will be critical to assess the burden of vaccine preventable diseases and affirm that blunting from maternal immunization has no material impact on disease control.

ABBREVIATIONS

Tdap: tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccine
VE: vaccine effectiveness

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