Epidemic Pertussis and Acellular Pertussis Vaccine Failure in the 21st Century

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In this issue of *Pediatrics* Acosta et al[1] present a tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis, adsorbed (Tdap) vaccine effectiveness study in adolescents in Washington State during the first 6 months of 2012. Their findings support the previous Tdap effectiveness data from Wisconsin.[2] The duration of Tdap effectiveness is disappointing, particularly because case-control studies tend to inflate efficacy.[3]

In 4 recent publications (including 1 article in *Pediatrics*) I have discussed epidemic pertussis and why vaccines fail.[4–7] Before discussing why Tdap vaccine effectiveness wanes so rapidly, it seems worthwhile to discuss how rapidly protection wanes after a natural infection in the pre-Tdap era and to take a realistic look at the resurgence of pertussis.

The resurgence of pertussis is often attributed to the switch from whole-cell pertussis vaccines to acellular products. However, the increase in reported pertussis began ~14 years before the universal use of diphtheria-tetanus-acellular pertussis (DTaP) vaccines in childhood commenced. The 2 greatest contributors to the resurgence of pertussis are greater awareness and more sensitive diagnosis (the routine use of polymerase chain reaction).[4–7]

In the pre-DTaP and -Tdap eras, the pertussis attack rate in nonepidemic periods in largely whole-cell pertussis vaccine–primed adolescents and adults was 370 to 500 per 100 000 per year.[8,9] These rates are underestimates because of clear evidence of "observer bias" in both studies.[10] In this present Washington State study, which involved adolescents 11 to 18 years of age, 81% of whom had received Tdap vaccines, the attack rate during the epidemic was only 182.3 per 100 000 for the one-half-year study period.[1] This rate is no greater than that noted during nonepidemic periods in the pre-DTaP and -Tdap eras.[8,9]

In 2012 in *Pediatrics* I discussed why pertussis vaccines fail[4]; however, new data have become available over the past 2 years. Of the 7 vaccine efficacy trials in the 1990s, in which diphtheria-tetanus toxoids-pertussis (DTP) vaccine efficacy was compared with DTaP vaccine efficacy, 5 different DTP vaccines were used. In 5 trials 4 different DTP vaccines from different manufacturers were more effective than the DTaP vaccines they were compared with. The only exception was 1 lot of US Connaught DTP vaccine, which was used in 2 trials; it was chosen because of its known low reactogenicity, but it was subsequently shown to lack immunogenicity and it had poor efficacy.

Factors that I think are most important relating to DTaP vaccine failure are as follows: decay in antibody over time; a T helper (Th) 1/Th2 versus a Th1, Th17 cellular response; incomplete antigen package; incorrect balance of antigens in the vaccine; linked-epitope suppression; and the occurrence of pertactin-deficient *Bordetella pertussis* strains.[4,11–18] Some, but not all, of these factors may also relate to Tdap failure over time.

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In contrast to children in whom antibody decay after vaccination (with both DTP and DTaP) or infection is relatively rapid, the antibody pattern in adolescents and adults is different.[19–23] In adolescents and adults after infection or vaccination the antibody values to pertactin, filamentous hemagglutinin (FHA), and fimbriae persist for a prolonged period, whereas antibody to pertussis toxin declines relatively rapidly.[21–23] This fact, as noted in the Adult Acellular Pertussis Vaccine Efficacy Trial (APERT) trial, led us to predict that an every-10-year booster program (if universally applied) could decrease the circulation of *B pertussis*.[23]

So why was our prediction that a 10-year booster would decrease the incidence and prevalence of pertussis wrong? In the microbiologic world there are a number of organisms that contain proteins similar to FHA, pertactin, and fimbriae.[24] In contrast, the only organism that has pertussis toxin is *B pertussis*. The persistence of antibody to FHA, pertactin, and fimbriae may be due to cross-reacting epitopes from other organisms, which our enzyme-linked immunosorbent assay picks up.[4] However, it seems apparent that the antibody values that we have determined do not offer much protection against *B pertussis* cough illness in adolescents and adults.

Although adequate data are presently not available, it can be assumed that adolescents and adults who were primed in infancy by infection or DTP will have a Th1, Th17 response to Tdap. In contrast, those who were primed by DTaP will have a Th1/Th2 response.

In line with the results of these 2 recent Tdap effectiveness studies, we should examine our present Tdap immunization recommendations. It is my opinion that we should continue with our present Tdap schedules. Of most importance is to see that all pregnant women receive Tdap with each pregnancy.[25,26] This alone can prevent virtually all pertussis deaths in young infants.

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