Physicians know that antibiotic use can increase strains of resistant microbes, and now it seems that vaccines might provide the same sort of selection pressure. The strains of Bordetella pertussis that are pertactin-deficient have increased from 14% in 2010 to 85% in 2012. Pertactin is thought to be involved in bacterial attachment to respiratory epithelium and to interfere with neutrophil-induced clearance of the pathogen. New work published this month in Pediatrics suggest the vaccines that include pertussis antigens are still effective, but show waning vaccine efficacy (VE).

The change suggests that the organism is evolving, a fact that worries public health professionals and pediatricians. That's because both of the currently used acellular pertussis vaccines contain pertactin as a component.

The vaccine administered for the primary series at two, four, and six months and booster doses at fifteen-eighteen months and four-six years of age is DTaP (diphtheria toxoid, tetanus toxoid and acellular pertussis). Booster doses for adolescents use Tdap (tetanus toxoid, reduced diphtheria and acellular pertussis). Those two vaccines replaced older whole-cell vaccines that had launched pertussis immunization program in the 1940s.

The evolution of pertussis organisms has taken place as numbers of cases increased, reaching 48,000 cases in 2012. Large numbers of those cases have occurred among children and adolescents who were fully vaccinated, often with only doses of the acellular vaccines. Questions have been raised about possible mechanisms for the waning immunity associated with use of the acellular vaccines. Suggested causes include less protective immune responses triggered by acellular vaccine, increased reporting and more sensitive diagnostic techniques (PCR vs. culture).

In addition, some researchers have suggested that the pertactin-deficient strains evolved because the vaccines induced a biological selection and provide a survival advantage for such strains. The question is whether the increase in pertactin-deficient strains is directly paralleled by the deceased vaccine effectiveness.

The Vermont research from Breakwell et al. (10.1542/peds.2015-3973) consists of two case-control studies on the two vaccines --DTaP and Tdap. That fact that the research was done in Vermont matters because that state had the second-highest incidence of pertussis in the US (103/100,000 population) and the state laboratory routinely cultured all suspected pertussis cases. Among available isolates, 90% were pertactin deficient. Those factors made Vermont an ideal place to assess the impact of pertactin deficiency on vaccine efficacy (VE).
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The researchers did two studies, one with children aged 4-10 years for DTaP, and a second for Tdap for older children and adolescents aged 11-19 years. Three controls were obtained for each child in both studies. The researchers assessed prior immunization histories by reviewing immunization records and parental interviews.

Overall VE for DTaP was 84% (95% CI 58-94%). VE for DTaP declined from 90% [95% CI, 71-97%] within 12 months of dose 5 (the final booster dose) to 68% [95% CI 10-88%] at 5-7 years post-vaccination. For Tdap, overall VE was 70% (95% CI, 54-81%). VE efficacy for Tdap declined from 76% (95% CI, 60-85%) at one-year post vaccination to 56% (95% CI 16-77%) at 2-4 years post-vaccination. Among the cases with available isolates, more than 90% were pertactin-deficient.

The study is an important one because it provides a warning that pediatricians and vaccine researchers can't be complacent about pertussis as it changes and evolves. The overall VE of 84% reported by the Vermont research for DTaP is similar to the 89% VE reported in California during the 2010 outbreak there. The overall Vermont VE reported for Tdap was 70%, a higher figure than the 64% VE reported during the 2012 pertussis outbreak in Washington State.

The proportion of pertactin-deficient strains in the California during the 2010 outbreak was 14% and the figure for Washington state during that outbreak was 76%.

This Vermont research is reassuring in that VE was documented for both DTaP and Tdap. But it is also concerning because pertactin-deficient strains are increasing. That raises the question of what other vaccine components (pertussis toxin, filamentous haemagglutinin or fimbriae) are preventing symptomatic transmission. The correlates of protection are not well-defined for pertussis.

In summary, both DTaP and Tdap vaccines have acceptable efficacy, but the changing organism will likely require newer vaccines and vigilant surveillance.

References


Further Reading

- Epidemic Pertussis and Acellular Pertussis Vaccine Failure in the 21st Century
- Predictors of Infant Death from Pertussis
- Pediatrics on Facebook