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

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COMPANION PAPER: A companion to this article can be found on page 981, and online at www.pediatrics.org/cgi/doi/10.1542/peds.2014-3358.

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.

REFERENCES

1. Acosta AM, DeBolt C, Tasslimi A, et al. Tdap vaccine effectiveness in adolescents during the 2012 Washington State pertussis epidemic. *Pediatrics*. 2015;135(6):981–989
2. Koepke R, Eickhoff JC, Ayele RA, et al. Estimating the effectiveness of tetanus-diphtheria-acellular pertussis vaccine (Tdap) for preventing pertussis: evidence of rapidly waning immunity and difference in effectiveness by Tdap brand. *J Infect Dis*. 2014;210(6):942–953
3. Fine PE, Clarkson JA. Reflections on the efficacy of pertussis vaccines. *Rev Infect Dis*. 1987;9(5):866–883
4. Cherry JD. Why do pertussis vaccines fail? *Pediatrics*. 2012;129(5):968–970
5. Cherry JD. Epidemic pertussis in 2012—the resurgence of a vaccine-preventable disease. *N Engl J Med*. 2012;367(9):785–787
6. Cherry JD. Pertussis: challenges today and for the future. *PLoS Pathog*. 2013;9(7):1–3
7. Cherry JD. The present and future control of pertussis. *Clin Infect Dis*. 2010;51(6):663–667
8. Strebel P, Nordin J, Edwards K, et al. Population-based incidence of pertussis among adolescents and adults, Minnesota, 1995-1996. *J Infect Dis*. 2001;183(9):1353–1359
9. Ward JI, Cherry JD, Chang SJ, et al; APERT Study Group. Efficacy of an acellular pertussis vaccine among adolescents and adults. *N Engl J Med*. 2005;353(15):1555–1563
10. Cherry JD, Heininger U, Stehr K, Christenson P. The effect of investigator compliance (observer bias) on calculated efficacy in a pertussis vaccine trial. *Pediatrics*. 1998;102(4 pt 1):909–912
11. Warfel JM, Zimmerman LI, Merkel TJ. Acellular pertussis vaccines protect against disease but fail to prevent infection and transmission in a nonhuman primate model. *Proc Natl Acad Sci USA*. 2014;111(2):787–792
12. Warfel JM, Merkel TJ. Bordetella pertussis infection induces a mucosal IL-17 response and long-lived Th17 and Th1 immune memory cells in nonhuman primates. *Mucosal Immunol*. 2013;6(4):787–796
13. Cherry JD, Heininger U, Richards DM, et al. Antibody response patterns to Bordetella pertussis antigens in vaccinated (primed) and unvaccinated (unprimed) young children with pertussis. *Clin Vaccine Immunol*. 2010;17(5):741–747
14. Storsaeter J, Hallander HO, Gustafsson L, Olin P. Levels of anti-pertussis antibodies related to protection after household exposure to Bordetella pertussis. *Vaccine*. 1998;16(20):1907–1916
15. Cherry JD, Gornbein J, Heininger U, Stehr K. A search for serologic correlates of immunity to Bordetella pertussis cough illnesses. *Vaccine*. 1998;16(20):1901–1906
16. Pawloski LC, Queenan AM, Cassiday PK, et al. Prevalence and molecular characterization of pertactin-deficient Bordetella pertussis in the United States. *Clin Vaccine Immunol*. 2014;21(2):119–125
17. Sheridan SL, Ware RS, Grimwood K, Lambert SB. Number and order of whole cell pertussis vaccines in infancy and disease protection. *JAMA*. 2012;308(5):454–456
18. Cherry JD, Olin P. The science and fiction of pertussis vaccines. *Pediatrics*. 1999;104(6):1381–1383
19. Blumberg DA, Mink CM, Cherry JD, et al. Comparison of an acellular pertussis-component diphtheria-tetanus-pertussis (DTP) vaccine with a whole-cell pertussis-component DTP vaccine in 17- to 24-month-old children, with measurement of 69-kilodalton outer membrane protein antibody. *J Pediatr*. 1990;117(1 pt 1):46–51
20. Guerra FA, Blatter MM, Greenberg DP, Pichichero M, Noriega FR; Pentacel Study Group. Safety and immunogenicity of a pentavalent vaccine compared with separate administration of licensed equivalent vaccines in US infants and toddlers and persistence of antibodies before a preschool booster dose: a randomized, clinical trial. *Pediatrics*. 2009;123(1):301–312
21. Heininger U, Cherry JD, Stehr K. Serologic response and antibody-titer decay in adults with pertussis. *Clin Infect Dis*. 2004;38(4):591–594
22. Hodder SL, Cherry JD, Mortimer EA Jr, Ford AB, Gornbein J, Papp K. Antibody responses to Bordetella pertussis antigens and clinical correlations in elderly community residents. *Clin Infect Dis*. 2000;31(1):7–14

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23. Le T, Cherry JD, Chang SJ, et al; APERT Study. Immune responses and antibody decay after immunization of adolescents and adults with an acellular pertussis vaccine: the APERT study. *J Infect Dis*. 2004;190(3):535–544

24. Mattoo S, Cherry JD. Molecular pathogenesis, epidemiology, and clinical manifestations of respiratory infections due to Bordetella pertussis and other Bordetella subspecies. *Clin Microbiol Rev*. 2005;18(2):326–382

25. Dabrera G, Amirthalingam G, Andrews N, et al. A case-control study to estimate the effectiveness of maternal pertussis vaccination in protecting newborn infants in England and Wales, 2012–2013. *Clin Infect Dis*. 2015;60(3): 333–337

26. Cherry JD. Tetanus-diphtheria-pertussis immunization in pregnant women and the prevention of pertussis in young infants. *Clin Infect Dis*. 2015;60(3): 338–340

REJUVENATING SLIME: *I was recently traveling in Myanmar and Thailand with a Thai friend in her early 50s. While we mostly spent nights in separate rooms, we shared a common room with my son while we were in a national forest in central Thailand. Each evening while there, she applied facial cream from a small tin. At home, I simply do not get involved with what my wife may or may not apply to her face, but here I was a bit intrigued – particularly when my friend told me the cream contained snail slime. At home, I consider snails a garden pest (or a delicacy to be eaten with garlic). When I pluck them off my brussels sprouts or lettuce, I usually have to spend a minute or two rinsing the slime off my hand.*

According to The Wall Street Journal *(A-Hed; February 27, 2015), snail slime has become a hot commodity in the international cosmetics market. The theory is that the slime, which evidently is packed with anti-oxidants and complex molecules, helps build skin collagen and restores skin to a more youthful appearance. Primarily extracted from South Korean snails, the product is a massive hit in South Korea and Japan and exploding in popularity in Thailand. It is so popular in Thailand that a local entrepreneur wants to develop Thai snail farms to help meet the local demand. He favors cultivation of* Hemiplecta distincta *which he claims makes a more potent mucous than snails raised in more temperate regions. However, harvesting the slime is not easy. While he envisions developing mechanical snail rubbers, currently it takes five people approximately four hours of snail rubbing to extract 20 liters of slime.*

While my friend certainly looked youthful, I was having a bit of trouble believing that her appearance was simply due to the rejuvenating power of snail slime. I opted not to bring any home with me for my lovely wife.

Noted by WVR, MD

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