

# Pertussis Immunization in the Global Pertussis Initiative North American Region

## *Recommended Strategies and Implementation Considerations*

Tina Tan, MD,\* Scott Halperin, MD,† James D. Cherry, MD,‡ Kathryn Edwards, MD,§  
Janet A. Englund, MD,|| Paul Glezen, MD,¶# David Greenberg, MD,\*\* Edward Rothstein, MD,††‡‡  
and Danuta Skowronski, MD§§

**Abstract:** In North America, children currently receive 5 doses of a combined diphtheria-tetanus-acellular pertussis vaccine between the ages of 2 months and 6 years. Although this schedule has reduced the incidence of childhood pertussis, it has not led to the development of herd immunity in the total population, largely because pertussis immunity wanes with time. The time course over which immunity wanes is uncertain; however, high pertussis antibody titers in adolescents and adults indicate unrecognized infection in these groups. There is evidence that this group serves as a source of infection for young infants who are not fully immunized. Therefore, of the potential strategies reviewed by the North American Global Pertussis Initiative group, universal adolescent immunization would in theory reduce the risk of pertussis in this age group and may reduce transmission to young infants. However, because immunity probably wanes at the same rate in adolescents and children, the burden of disease will likely shift to older age groups, including young adults (parents of vulnerable infants). Therefore the ideal would be immunization of adolescents and adults, particularly those who are in contact with young infants. Adolescent

immunization is already recommended in Austria, France, Germany and Canada, and participants in the Global Pertussis Initiative recommend that this strategy be implemented across North America with a view to eventually extending immunization to include adults. The final decision to implement such a strategy will depend on pertussis surveillance studies and analysis of the effectiveness and tolerability of adolescent and adult pertussis immunization as well as program considerations related to feasibility and economics.

**Key Words:** *Bordetella pertussis*, pertussis, disease, immunization, adolescents, adults, United States, Canada

(*Pediatr Infect Dis J* 2005;24: S83–S86)

In many countries, despite highly effective childhood immunization programs, infection with *Bordetella pertussis* continues to pose a public health threat. In the United States, 2.7 cases/100,000 population were recorded in 2000, which is almost 3 times the target set by the World Health Organization of less than 1 case/100,000 population.<sup>1</sup> Data from 2002 in the United States report an even higher incidence (3.4 cases/100,000 population).<sup>2</sup> Furthermore these figures are an underestimate given that cases of pertussis in adolescents and adults often go undiagnosed. North American studies suggest that 20–25% of cases of persistent cough are the result of infection with *B. pertussis*.<sup>3–5</sup>

Mass immunization programs that use the widely available whole cell pertussis and acellular pertussis (aP) vaccines have significantly reduced the incidence of pertussis among children and associated childhood mortality.<sup>1</sup> However, if childhood immunization programs had led to the development of complete herd immunity, they would also protect infants under the age of immunization (2–3 months)<sup>6</sup>; but this is not the case, and waning immunity has reduced the overall effectiveness of these programs. The duration of protection postvaccination is 5–10 years,<sup>7–9</sup> and the waning of immunity leaves adolescents and adults vulnerable to infection with *B. pertussis*, making them a source of infection for young infants, other adolescents and adults.

From the \*Division of Infectious Diseases, Northwestern University's Feinberg School of Medicine, The Children's Memorial Hospital, Chicago, IL; †Dalhousie University, Halifax, Nova Scotia, Canada; the ‡Department of Pediatrics, UCLA School of Medicine, Los Angeles, CA; the §Division of Pediatric Infectious Diseases, Department of Pediatrics, Vanderbilt University Medical Center, Nashville, TN; the ||Division of Infectious Diseases, Children's Hospital and Regional Medical Center, Seattle, WA; the ¶Preventive Medicine Section, Department of Pediatrics, and the #Department of Molecular Virology and Microbiology, Baylor College of Medicine, Houston, TX; the \*\*University of Pittsburgh School of Medicine, Division of Allergy, Immunology and Infectious Diseases, Children's Hospital of Pittsburgh, Pittsburgh, PA; ††Pennridge Pediatric Associates, Sellersville, PA and ‡‡Temple University School of Medicine, Philadelphia, PA; and §§Epidemiology Services, BC Center for Disease Control, Vancouver, British Columbia, Canada

Address for correspondence: Dr Tina Q. Tan, Feinberg School of Medicine, Northwestern University Division of Infectious Disease, Children's Memorial Hospital, 2300 Children's Plaza, Box 20, Chicago, IL 60614-3394. E-mail titan@childrensmemorial.org.

Copyright © 2005 by Lippincott Williams & Wilkins

ISSN: 0891-3668/05/2405-0083

DOI: 10.1097/01.inf.0000160919.94330.1a

In 2001, the Global Pertussis Initiative (GPI) was established as an expert scientific forum to analyze the status of pertussis disease globally and to evaluate immunization strategies to improve disease control. These goals were identified with the final objective of protecting infants who are not yet fully immunized.<sup>10</sup> GPI participants from the United States and Canada concluded that universal adolescent immunization was the most appropriate first step, with a view toward eventually immunizing adults, focusing initially on, but not limited to: new parents; close contacts of newborns; health care workers; and child care workers.

The selected strategies are discussed in detail here, as are the possible obstacles to implementation of the strategies. Other strategies evaluated by the GPI participants and those recommended by the European and international regions are described elsewhere in this supplement.<sup>11–13</sup>

The strategy of universal adolescent immunization aims to reduce morbidity caused by pertussis disease in adolescents, contribute to herd immunity, and reduce transmission of *B. pertussis* to unimmunized or incompletely immunized infants. The GPI participants do not aim to implement changes to countries' immunization strategies. Rather the group aims to raise awareness of pertussis through its recommendations and seek consideration by the appropriate authorities as policy and immunization recommendations are evaluated.

## CURRENT IMMUNIZATION SCHEDULES

Current immunization programs in the United States and Canada comprise a primary course of the combined diphtheria-tetanus-acellular pertussis (DTaP) vaccine. In the United States, the initial course consists of 3 immunizations with DTaP vaccine at 2, 4 and 6 months of age followed by boosters at 15–18 months and at 4–6 years. In Canada, the DTaP vaccine is administered as a pentavalent combination as DTaP-inactivated poliovirus (IPV)-*Haemophilus influenzae* type b vaccine at 2, 4, 6 and 18 months with a quadrivalent booster of DTaP-IPV at 4–6 years of age. An adolescent/adult formulation of dTaP was licensed in Canada in 1999 with a view to extending the duration of protection. By the spring of 2002, Newfoundland and Nunavut alone had implemented an adolescent booster program; but by the fall of 2004, all provinces and territories of Canada had followed suit. In general, adolescent booster in Canada has replaced the preexisting Td schedule, the timing of which has historically varied across provinces. Currently Tdap is administered in Canada between grade 8 (13–14 years of age) and grade 10 (15–16 years of age) with most provinces offering the vaccine in grade 9 (14–15 years of age).

## RECOMMENDED STRATEGIES TO OVERCOME PERTUSSIS DISEASE

*United States.* After lengthy discussion and final voting, the North American participants recommended that an aP vaccine be incorporated into the current U.S. immunization schedule for diphtheria-tetanus vaccine (dT) that is provided to adolescents 11 years of age or older. The vaccine could be administered

either as dTaP or as an additional stand alone aP booster for adolescents up to date with their dT immunization. Thus all 11- to 18-year-olds would be immunized against diphtheria, tetanus and pertussis.

*Canada.* A shift in the age distribution of pertussis toward preteens and teens has been observed in several provinces of Canada. This has been attributed in part to waning immunity and/or a moving cohort effect among children who received a whole cell pertussis vaccine for childhood doses. The contribution of changes in diagnostic approaches has also been acknowledged.<sup>14,15</sup> The shift in age distribution has led to the replacement of whole cell combination vaccines by acellular pertussis formulations for childhood doses (2, 4, 6, 18 months and 4–6 years of age) across Canada in 1997–1998 and subsequently to the introduction of an adolescent acellular pertussis booster dose, implemented by all provinces and territories across Canada by the fall of 2004. The impact of these immunization changes on the burden of disease and the age distribution of pertussis in Canada is currently being monitored through surveillance activities. Recommendation for routine adult pertussis immunization is pending the results of ongoing surveillance and further information on the anticipated impact and safety of repeat doses, their optimal targeting and spacing across the lifespan.

Although pertussis is a problem in adults in North America, some of the GPI participants thought that there are insufficient data to support current immunization of all adults. Therefore an adult strategy may focus on specific adult subgroups such as young adults and new parents, close contacts of newborns, health care workers and child care workers. An immunization program in targeted adult subgroups is unlikely to have an effect on the epidemiology of pertussis and thus is less of a public health intervention than a personal protection strategy. There are no data to support the immunization of parents and other close contacts of newborns, but this is a logical strategy and there is no risk associated with the intervention.

The North American Global Pertussis Initiative participants suggested that adolescent immunization is simply the first step toward achieving universal adolescent and adult immunization. Groups of adults who could be targeted initially could include new parents, people in close contact with young infants, such as other family members, and health care and child care workers.

## RESEARCH NEEDED TO SUPPORT RECOMMENDED STRATEGIES

Pertussis is still widely perceived to be an infant disease. Practitioners do not generally consider pertussis when diagnosing adolescent or adults, leading to significant underreporting of the disease, particularly in adults and adolescents.<sup>16,17</sup> Accurate information on the true incidence of the disease is required for physicians, health authorities, health insurers and the general public to understand the need for universal adolescent immunization (or immunization of adults). To obtain this information, standardized laboratory techniques must be made widely available, and surveillance techniques must be improved. Of particular use would be the establishment of linked disease-vaccine

registries to monitor the incidence of pertussis among immunized and nonimmunized populations.

More information on the duration of immunity provided by both childhood and adolescent aP vaccines will enable boosters to be timed for optimal effect. Because individuals would likely be required to have several aP immunizations in a lifetime, an accurate tolerability profile of the sixth and subsequent boosters is necessary.

In addition, studies of the feasibility of eliminating the pertussis booster dose at 2 years of age must be performed. Also to be considered is the elimination of the 6-month injection, rather than the booster (similar to the Swedish schedule of a 2-dose primary immunization and a booster in the second year of life). Ongoing correlates of immunity studies and extensive household contact studies with available data on cell-mediated immunity and antibody titers before exposure are also needed.

Research into the impact of adolescent and adult immunization on transmission to infants is needed to support the ongoing implementation of these strategies. Data are additionally required to demonstrate the population effectiveness of strategies targeted at specific subgroups. In addition, immunization as a condition of employment (eg, health care and child care workers) cannot be supported in the absence of appropriate vaccine efficacy and epidemiologic data.

## POTENTIAL OBSTACLES TO IMPLEMENTING RECOMMENDED IMMUNIZATION STRATEGIES

*Availability of Appropriate Vaccines.* No dTaP vaccine is currently licensed for use in adolescents in the United States, but one is available in Canada; no stand alone aP vaccine is available in either country. Until a dTaP vaccine is available in the United States, neither universal adolescent nor adult immunization can be implemented. Research, development and clinical testing of a stand alone vaccine are ongoing.

*Access to Target Populations.* One strategy to ensure that adolescents are immunized against pertussis is to immunize them when they receive a dT booster. Compliance is enhanced by requiring immunization for school entry. In Canada, school-based immunization programs are widely accepted; but in the United States, immunizations are more often administered by physicians at routine clinic visits. Thus education of physicians and parents will be of particular importance to the success of the strategy in the United States. Experience from influenza immunization shows that compliance with these types of programs is low; in the absence of robust data on the benefits of immunization, this is unlikely to be any greater for pertussis programs. Given that adult pertussis vaccination, if routinely recommended, will likely be administered as dTaP replacement of currently recommended adult Td boosters, efforts to understand the determinants and deterrents of current uptake in adults in anticipation of recommended pertussis programs are under way.<sup>18</sup>

If immunization is to be extended beyond adolescents, access to the target population will be more difficult. Possible

mechanisms by which adults could be targeted include occupational health programs and hospital-based epidemiology programs. Experience from influenza immunization shows that compliance with these types of programs is low; in the absence of robust data on the benefits of immunization, this is unlikely to be any greater for pertussis programs.

Large scale public health education programs would be needed to convince other groups of adults of the benefits of pertussis immunization, such as those in close contact with young infants (eg, parents and relatives). Gaining access to this group would also be difficult, although parents would be relatively easy to contact. Obstetricians and nurse midwives would be ideally placed to promote the importance of immunization to these close contacts of newborns. Moreover, a strategy of immunization of women in late pregnancy to give newborns protection through transplacental antibodies is worthy of exploration, as the safety and efficacy of influenza and other vaccinations in this group is already well documented.<sup>19</sup>

*Availability of Appropriate Delivery Infrastructures.* The delivery of vaccine is not a major barrier to the implementation of adolescent pertussis immunization since a delivery infrastructure is already in place for dT vaccines, via either schools or routine visits to pediatricians. However, it could be improved in regions that do not require immunization before high school entry.

Vaccine delivery to subgroups of adults, such as health care and child care workers, may be feasible on entry into training or employment. However, given the age that this might occur, this should be coordinated with adolescent booster immunization. Household and family contacts with young infants may be a harder population to target, as this approach does not complement any other schedule that is currently in use.

For any expanded immunization program, intensive education of physicians, nurses, other health care providers, government agencies and insurers will be necessary to ensure effective delivery, after research to demonstrate the effectiveness of these education programs.

*Diagnosis and Surveillance.* Pertussis is unlikely to be accurately diagnosed or reported if neither the general public nor health care professionals are sufficiently aware of the disease or, if they are aware of it, they do not have access to reliable diagnostic methods. Large scale education programs are needed to raise awareness of pertussis disease and the importance of immunization among physicians and other health care professionals. Improvements in laboratory diagnostic methods should include the availability and easy accessibility of routine polymerase chain reaction and/or single specimen antibody tests. Both polymerase chain reaction and serologic assays, where routinely applied, have contributed to a fuller understanding of the epidemiologic profile of pertussis, and, in particular, the impact of pertussis in older age groups.<sup>14</sup> A new rapid, widely accepted and readily available diagnostic test is needed. Improved surveillance systems will also be needed to monitor the impact of any adolescent and adult immunization programs.

*Resources, the Health Care Agenda and Policy Makers.* It is acknowledged that there would be a financial consideration if pertussis immunization strategies were expanded.

Economic modeling to demonstrate the cost effectiveness of adolescent immunization, combined with epidemiology data from the areas of Canada where this strategy is already being implemented, should help to inform pertussis immunization programs.<sup>20</sup> Further cost effectiveness studies must be conducted. Similarly reimbursement and insurance issues must be addressed as soon as such data become available.

*Education and Awareness.* Because pertussis is no longer perceived by the general public and health care professionals to be a serious disease, education programs aimed at health care professionals who treat adolescents and adults will play a central role in the acceptance of new immunization strategies. However, education programs must be based on reliable data. Of particular importance are data on the incidence of pertussis in adolescent and adult populations, and the transmission of disease to unimmunized or incompletely immunized infants. Data are required, too, to show the effectiveness of targeted immunization in comparison with universal immunization. Such data are needed to convince groups of experts who influence the content and structure of immunization programs at the level of national government about the importance of pertussis. Improved diagnosis and surveillance will make a major contribution to both education and awareness.

## CONCLUSION

Of the strategies evaluated by GPI participants, universal adolescent immunization is currently the first step to extend coverage of current immunization schedules in the United States and Canada. Indeed adolescents in all provinces and territories of Canada have benefitted from publicly funded dTaP programs since the fall of 2004, conveniently implemented as replacement doses for previous Td boosters. Phase IV, postmarketing evaluations of the tolerability and impact of adolescent programs in Canada will provide important data to inform future global developments with respect to pertussis immunization. It is therefore possible that this strategy may be extended to include specific target groups within the adult population to extend the duration of protection, assuming the availability of data to show the effectiveness of targeted immunization.

The perception of pertussis as a low risk illness is one of the main obstacles to an extension of North American immunization programs to adolescents and, eventually, adults. Effective childhood pertussis immunization programs have reduced the incidence of serious cases of the disease to sufficiently low levels that it is no longer perceived to be a significant public health problem. However, pertussis continues to pose a serious threat to the lives of young infants who are unimmunized or incompletely immunized.<sup>21</sup>

Improved awareness of pertussis as a major public health problem will encourage adolescents and adults to seek treatment of persistent cough and will improve diagnostic accuracy. Improved detection should also lead to a more accurate estimate of

the true incidence of the disease. Disease registries would be particularly useful in this respect. Without such data, it is difficult to measure the true impact, in particular the cost effectiveness, of any immunization strategy. Moreover such data may eventually lead to a change in the timing of pertussis boosters to provide optimal protection. However, the GPI participants feel that adolescent immunization should be encouraged now on the basis of existing data to prevent further pertussis-related morbidity in teens themselves and possibly also mortality in the most vulnerable, infants.

## REFERENCES

1. World Health Organization. Pertussis surveillance: Global Meeting; October 16–18, 2000; Geneva, Switzerland. Available at: [www.who.int/vaccines-documents/DocsPDF01/www605.pdf](http://www.who.int/vaccines-documents/DocsPDF01/www605.pdf).
2. Centers for Disease Control and Prevention. Summary of notifiable diseases, United States, 2002. *MMWR*. 2004;51:1–84.
3. Mink CM, Sirota NM, Nugent S. Outbreak of pertussis in a fully immunized adolescent and adult population. *Arch Pediatr Adolesc Med*. 1994;148:153–157.
4. Senzilet LD, Halperin SA, Spika JS, Alagaratnam M, Morris A, Smith B. Pertussis is a frequent cause of prolonged cough illness in adults and adolescents. *Clin Infect Dis*. 2001;32:1691–1697.
5. Wright SW, Edwards KM, Decker MD, Zeldin MH. Pertussis infection in adults with persistent cough. *JAMA*. 1995;273:1044–1046.
6. Wendelboe AM, Van Rie A, Salmaso S, Englund JA. Duration of immunity against pertussis after natural infection or vaccination. *Pediatr Infect Dis J*. 2005;24(suppl):S58–S61.
7. He Q, Viljanen MK, Nikkari S, Lyytikäinen R, Mertsola J. Outcomes of *Bordetella pertussis* infection in different age groups of an immunized population. *J Infect Dis*. 1994;170:873–877.
8. Fine PE, Clarkson JA. Reflections on the efficacy of pertussis vaccines. *Rev Infect Dis*. 1987;9:866–883.
9. Jenkinson D. Duration of effectiveness of pertussis vaccine: evidence from a 10-year community study. *Br Med J (Clin Res Ed)*. 1988;296:612–614.
10. Plotkin S. Global Pertussis Initiative: process overview. *Pediatr Infect Dis J*. 2004;24(suppl):S7–S9.
11. Forsyth K, Nagai M, Lepetic A, Trindade E. Pertussis immunization in the Global Pertussis Initiative international region: recommended strategies and implementation considerations. *Pediatr Infect Dis J*. 2005;24(suppl):S93–S97.
12. Forsyth K, Tan T, Wirsing von König CH, Caro J, Plotkin S. Potential strategies to reduce the burden of pertussis. *Pediatr Infect Dis J*. 2005;24(suppl):S69–S74.
13. Wirsing von König CH, Campins-Marti M, Finn A, Guiso N, Mertsola J, Liese J. Pertussis immunization in the Global Pertussis Initiative European region: recommended strategies and implementation considerations. *Pediatr Infect Dis J*. 2005;24(suppl):S87–S92.
14. Skowronski DM, De Serres G, MacDonald D, et al. The changing age and seasonal profile of pertussis in Canada. *J Infect Dis*. 2002;185:1448–1453.
15. Nteyayabo B, De Serres G, Duval B. Pertussis resurgence in Canada largely caused by a cohort effect. *Pediatr Infect Dis J*. 2003;22:22–27.
16. Farizo KM, Cochi SL, Zell ER, Brink EW, Wassilak SG, Patriarca PA. Epidemiological features of pertussis in the United States, 1980–1989. *Clin Infect Dis*. 1992;14:708–719.
17. Yaari E, Yafe-Zimmerman Y, Schwartz SB, et al. Clinical manifestations of *Bordetella pertussis* infection in immunized children and young adults. *Chest*. 1999;115:1254–1258.
18. Skowronski DM, Pielak K, Rempel VP, et al. Adult tetanus, diphtheria and pertussis immunization: knowledge, beliefs, behavior and anticipated uptake. *Vaccine*. 2004;23:353–361.
19. Munoz FM, Greisinger AJ, Wehman OA, et al. Safety of influenza vaccination during pregnancy. *Am J Obstet Gynecol*. 2005; in press.
20. Caro J, Getsios D, El-Hadi W, Payne K, O'Brien JA. Pertussis immunization of adolescents in the United States: an economic evaluation. *Pediatr Infect Dis J*. 2005;24(suppl):S75–S82.
21. Centers for Disease Control and Prevention. Pertussis, United States, 1997–2000. *MMWR*. 2002;51:73–76.