Prevention of Pertussis among Adolescents by Vaccination: Taking Action on What We Know and Acknowledging What We Do Not Know

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(See the article by Purdy et al. on pages 20–8)

Pertussis is the only disease for which children are routinely vaccinated that is not at historically low levels in the United States. The increases seen in pertussis are not due to ineffective vaccines or programs. The effectiveness of acellular pertussis vaccine has been demonstrated to be high in both prelicensure studies and postlicensure evaluations, and coverage among vaccine-eligible age groups remains high. However, pertussis continues to strike those who are susceptible because of waning vaccine-induced immunity and infants who are too young to have completed the primary vaccination series. To address the issue of waning immunity, formulations of acellular pertussis vaccine combined with diphtheria and tetanus toxoids for adolescents and adults (TdaP) are now under development in the United States; TdaP vaccines are already licensed and available in Canada, Germany, France, and Australia and are expected in the United States soon. Because a vaccine to prevent pertussis in older children, adolescents, and adults is likely to be available soon, how should policy makers approach its use?

Our recommendations for use of TdaP should be guided by our knowledge, and there are things we know well about pertussis. Outbreaks of pertussis occur in a variety of settings but are most frequently recognized in middle and high schools. Antimicrobial prophylaxis is recommended for close contacts of patients with pertussis, and outbreak response is a complex, costly, and disruptive activity for schools and local health authorities. The rates of hospitalization, serious complications, and death among adolescents are low, but cough illness due to pertussis is prolonged, and the health impact—in terms of medical visits, antimicrobial treatment, and experience of illness—is significant. Currently, these school-based outbreaks are not preventable, and the only strategies for control are identification, isolation, and prophylaxis of contacts.

But there is much that is not known about pertussis. It is unclear whether the recent increases in reported disease are real or are artifacts of increased recognition; the increase in reported cases among young infants, coupled with relatively stable rates of reported disease among older infants and preschool-aged children, suggests that there may be a real increase in the circulation of Bordetella pertussis in some age groups [1]. But there is no doubt that ascertainment of pertussis is variable and incomplete in most age groups. Physicians may not consider the diagnosis, especially in adolescents and adults, because of a lack of clinical awareness that pertussis occurs in these age groups. Diagnostic testing is imperfect, and some tests have not been well standardized. Culture of B. pertussis remains the gold standard by which other assays are judged, but unless the diagnosis is considered early in the course of illness and before administration of antimicrobial therapy, isolation of the bacterium is unlikely. Serological testing, once standardized, may facilitate diagnosis, but it remains unavailable in most areas, and assays based on PCR are variable in sensitivity and specificity [2]. Thus, our knowledge of the burden of pertussis is far from complete.

There is also much that we do not know about the dynamics of B. pertussis transmission. It is unclear what impact vaccinating young adolescents would have on disease incidence in other age groups. Do middle and high schools, with their high contact rates and susceptible populations, amplify B. pertussis circulation in the community? If routine vaccination of young adolescents prevented those out-
breaks but immunity was not long-lasting, would outbreaks then occur among young adults? Would transmission to young infants—the group with the highest morbidity and mortality due to pertussis—decrease or increase following implementation of an adolescent pertussis vaccination program? Mathematical modeling suggests that the impact of routine adult pertussis vaccination on the incidence of pertussis in young children may be relatively modest [3].

Because of these and other uncertainties, estimating the impact of pertussis vaccination of adolescents and adults on disease burden requires many assumptions. Purdy et al. [4] have explicitly stated the assumptions underlying their estimates of costs and benefits; given that all scenarios that they examined were reported as having break-even costs of $28–$37, it is worth looking closely at those assumptions. The model is most sensitive to changes in vaccine coverage, pertussis incidence, and indirect costs. Vaccination of adults remains challenging, and adolescent vaccination coverage lags substantially behind childhood coverage. Well-designed studies have demonstrated that pertussis is more common than generally appreciated among adults, but data on pertussis incidence in older age groups are very limited; extrapolating rates derived from persons 40–49 years of age—who may be more likely than older adults to have adolescents in the household—may result in significant overestimates of pertussis incidence among older adults. Data on direct and indirect costs of pertussis are limited, and cost estimates derived from recognized cases of pertussis may or may not be applicable to the larger number of unrecognized cases; more-typical—and more-severe—cases of pertussis are probably more likely to be diagnosed and reported than are milder cases. Finally, Purdy et al. [4] note that few adverse events have been observed after acellular pertussis vaccination in adolescents and adults. Because of the recognition of limb swelling following fourth and fifth doses of acellular pertussis vaccines in children, limb swelling could occur much more frequently among adolescents or adults who received acellular pertussis vaccine, rather than whole-cell pertussis vaccine, in childhood. Thus, the assumptions about adverse events following vaccination of adolescents and adults may need to be reevaluated in the context of a 6-dose series of acellular pertussis vaccine.

The acellular pertussis vaccine likely will be available for use in adolescents and adults before many of these questions are answered, and policy makers will have to make decisions about how to use a Tdap vaccine, once it is available, in the absence of certainty. A cost-benefit analysis is one consideration, but others include vaccine safety, efficacy, and acceptability; public health impact of the disease; and feasibility of program implementation. A recommendation aimed at vaccination of young adolescents would likely be considered feasible. Such a recommendation would be compatible with existing childhood and adolescent recommendations and could be implemented at the recommended early adolescent immunization visit. Postlicensure evaluation of the safety of acellular pertussis vaccines, when administered as a 6-dose series, will be needed.

How will the vaccine be used in the United States? Policy makers will probably closely focus on the burden of disease that could be prevented among adolescents; although no decisions have yet been made, a recommendation to vaccinate young adolescents for prevention of pertussis is most consistent with what we know about pertussis. Outbreaks of pertussis do occur in middle and high schools. School-based outbreaks probably occur more frequently than we know; the differences in reported pertussis incidences among states are largely due to differences in rates of reported disease among older age groups [5]. In contrast, the disease burden for adults is more uncertain, and implementation of a recommendation for routine adult booster vaccination would present significant challenges. As new tools become available for prevention of pertussis, we will have an opportunity to take action on what we know, to monitor the impact of our interventions, and, at the same time, to continue to work to better understand the things we do not know.

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References