Diphtheria, Tetanus, and Pertussis: Unequal Vaccine Siblings With Distinct Characteristics

TO THE EDITOR—With great interest I read the article by Slifka et al [1] who reported convincing evidence that performing regular booster vaccinations against diphtheria and tetanus in adults does not provide benefits. Yet, several countries still recommend diphtheria and tetanus boosters every 10 or 20 years, most likely based on convenience (as the decimal system allows us to remember round numbers easily) than immunology.

The evidence with respect to diphtheria and tetanus boosters is in stark contrast to the apparent need for pertussis vaccine boosters, which an increasing number of countries—such as the United States—recommend at least once for adults and in every pregnancy [2, 3]. The rationale for pertussis vaccine booster doses in every pregnancy is to provide the fetus with optimal amounts of anti-pertussis toxin antibodies. These specific antibodies protect young infants from life-threatening pertussis before they can develop their own immunity via the primary immunization series commencing at 6–8 weeks of age [4, 5]. Unfortunately, there is no licensed stand-alone acellular pertussis vaccine available (except in Thailand [6]), so that pertussis immunization can only be performed together with tetanus and diphtheria toxoid antigens by use of tetanus, diphtheria, and acellular pertussis (Tdap) combination vaccines [2]. These extra doses of diphtheria and tetanus vaccines clearly are superfluous both for the pregnant women and their unborn children in utero.

When looking back at the history of pertussis combination vaccines it becomes evident that Tdap was not developed for use in adults first [7]. In the late 1980s, several acellular component combination vaccines (diphtheria, tetanus, and pertussis [DTaP]) were developed because of serious safety concerns

with DTwP. In the early 1990s, they were tested, then licensed and consequently introduced in immunization programs for infants in most high-income countries to substitute for whole cell component combination vaccines (diphtheria, tetanus, and pertussis [DTwP]) products [8]. Further on, in the late 1990s, diphtheria-tetanus-acellular pertussis combination vaccines with reduced diphtheria toxoid antigen (termed Tdap) were developed to booster immunity with 1 injection against all 3 diseases, first in toddlers and then in adolescents and adults [9]. Today, with the evidence provided by Slifka et al in this Journal [1], it is evident that diphtheria, tetanus, and pertussis are unequal vaccine siblings combined in Tdap but with distinct characteristics and distinct needs for booster doses. Therefore, it is time to request stand-alone pertussis vaccines on a large scale for optimal use in adults, especially in pregnant women, independent of diphtheria and tetanus toxoids [7].

Note

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Reply to Heininger

TO THE EDITOR—We thank Dr Heininger for his comments and for the opportunity to discuss the implications of modifying adult booster vaccination schedules as well as the importance of pertussis vaccination among pregnant mothers. Although pertussis is relatively benign among healthy adults, it can be a severe and life-threatening disease among infants. The World Health Organization (WHO) recommends that women receive Tdap (tetanus, diphtheria, acellular pertussis) vaccination during pregnancy to increase the transfer of protective *Bordetella pertussis*-specific

maternal antibodies to their newborns [1]. Indeed, maternal Tdap vaccination during pregnancy has been shown to reduce infant pertussis risk by $\geq 90\%$ [2, 3] and is 85% more effective than postpartum Tdap vaccination of mothers at preventing infant pertussis [4].

The United States currently recommends that adults receive Td (tetanus, diphtheria) vaccination every 10 years and that at least 1 Td vaccination be substituted with Tdap in an effort to reduce pertussis transmission to infants [5]. However, it is unclear if Tdap vaccination of the general adult population is effective at combating this infant disease since the efficacy of focused vaccination efforts on parents and close family members (referred to as “cocooning”) has been inconclusive [5]. Vaccination of mothers postpartum does not reduce the rate of pertussis among infants [6]. In a study of 53 149 infants, there was no difference in pertussis rates among infants whose parents were both vaccinated postpartum compared with those with unvaccinated parents (1.9 vs 2.2 infections per 1000 infants, respectively) [7]. Together, this indicates that maternal vaccination during pregnancy may be a more effective approach than cocooning to reduce the risk of infant pertussis.

As Dr Heininger noted, there is currently no licensed stand-alone acellular pertussis vaccine in routine use, and many countries therefore recommend Tdap at each pregnancy [8]. Our study indicates that routine/scheduled Td booster vaccinations among adults may be unnecessary for maintaining immunity against these 2 diseases [9]. However, we agree with Dr Heininger, the WHO [1], and the Centers for Disease Control and Prevention [5] on the importance for women to receive pertussis vaccination during pregnancy to protect against infant pertussis. One caveat, however, is the potential for increased adverse reactions with repeated Tdap administrations for multiple pregnancies. In one prospective cohort study, 11.4% of pregnant women who had been vaccinated within the previous 3–4 years experienced local reactions compared

with 6.0% of women who had not been vaccinated during this period of time [10]. Although it is unclear if manufacturers will find it cost-effective to produce a stand-alone acellular pertussis vaccine for pregnant women, the development of this type of vaccine could reduce vaccine-associated adverse events and is worthy of further investigation. Discontinuation of routine/decennial Td and Tdap boosters among most fully vaccinated adults may also help to reduce the total number of recent vaccinations and increase the time interval between the last booster dose and the first pregnancy as a means to further mitigate potential vaccine-related adverse events.

Notes

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Bacterial Coinfection in Adults With Severe Malaria

To THE EDITOR—Approximately 6.4% of children with severe malaria in malaria-endemic regions have concomitant bacteremia [1]. As coinfecting children have a higher mortality and their bacterial infection may be difficult to diagnose, international guidelines recommend that they receive both antimalarial and empirical broad-spectrum antibacterial therapy [2]. The same guidelines state that adults with severe malaria should not receive empirical antibacterial therapy [2]. There have been few published data to support this recommendation and so the work by Phu et al—which identified concomitant bacteremia in only 9/845 (1.07%) Vietnamese adults with severe malaria—is very welcome [3].

However, their figure of 1.07% is likely an underestimate. For most of their 1991–2003 study, manual blood cultures were collected, which the authors acknowledge may have a lower sensitivity. From September 1997 they did use BACTEC-plus® bottles, but collected a suboptimal 5–8 mL of blood. They assert that prior antibacterial therapy—which