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Cherry, James D

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Tetanus-Diphtheria-Pertussis Immunization in Pregnant Women and the Prevention of Pertussis in Young Infants

James D. Cherry

Department of Pediatrics, David Geffen School of Medicine, University of California, Los Angeles

(See the Major Article by Dabrera et al on pages 333–7.)

Keywords. pertussis; Tdap; immunization; pregnancy.

A case-control study from England and Wales on the effectiveness of tetanus-diphtheria-pertussis (Tdap) immunization in pregnant women, authored by Dabrera et al in this issue of *Clinical Infectious Diseases*, supports the finding of a previous observational study done by the same group of investigators [1, 2]. As noted by the authors, a single dose of Tdap was recommended in the United Kingdom for pregnant women between 28 and 38 weeks' gestation in October 2012. In the United States, the Advisory Committee on Immunization Practices (ACIP) made a similar recommendation in October 2011.

One aspect of the UK experience with Tdap vaccination of pregnant women is noteworthy—that in England and Wales, pregnant women typically receive care by general practitioners, and these same practitioners are routinely responsible

for immunization of all their patients. The present study was carried out between 22 October 2012 and 11 July 2013. Therefore, it was conducted over a 9-month period that started just 3 weeks after Tdap was recommended for pregnant women. Nevertheless, approximately 64% of the pregnant women were vaccinated.

In contrast with the experience in England and Wales, the Tdap program in the United States is struggling, even though it was recommended a full year before the recommendation was made in the United Kingdom [3, 4]. Both Harriman and Winter [4] and Housey et al [3] note some of the difficulties with implementing prenatal vaccination in the United States. For example, in an October 2013 survey of women delivering in California hospitals, only 25% had received Tdap during pregnancy. Also, in contrast with the United Kingdom where general practitioners routinely administer vaccines, there are a number of barriers relating to vaccine use in obstetrical practices in the United States. These are mainly financial barriers such as the up-front cost of ordering and storing vaccines, maintaining vaccine inventory, and, most important, inadequate reimbursement [4]. There clearly is something wrong with the US system when 25% of claims are not

paid by insurance companies. However, it is encouraging to note that in the fourth quarter of 2013, >65% of pregnant women in the Northern California Kaiser system had received Tdap. This was possibly because the vaccine was available in all obstetric clinics.

At the University of California, Los Angeles (UCLA) Medical Center, an observant pediatrician noted that most of the mothers of the babies she was seeing had not been offered Tdap during their pregnancy (Heidi Woo, personal communication). Following her observation, the UCLA health system ensured that all UCLA obstetrical offices are stocked with Tdap vaccines. Rates of Tdap immunization in obstetric practices at UCLA are now being studied.

A concurrent issue is influenza vaccination of pregnant women. Ten years ago, ACIP and the American College of Obstetricians and Gynecologists recommended influenza vaccination for all women who are or will be pregnant during the influenza season [5]. In the 2012–2013 influenza season, only 50.5% of women received influenza vaccine either before or during pregnancy. As with Tdap, financial barriers are cited by obstetricians as an impediment to influenza vaccination of pregnant women [5].

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Correspondence: James D. Cherry, MD, MSc, Department of Pediatrics, David Geffen School of Medicine at UCLA, 10833 Le Conte Ave, MDCC 22-442, Los Angeles, CA 90095 (jcherry@mednet.ucla.edu).

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During the last 10 years, a number of pertussis epidemics have occurred in the United States [6]. Although the numbers of cases have been inflated because of greater awareness of pertussis and the use of polymerase chain reaction testing, it is clear that diphtheria-tetanus-acellular pertussis (DTaP) vaccines are not as effective as the whole-cell vaccines [6–12]. A number of factors explain why immunity conferred by our presently used DTaP and Tdap vaccines wanes more rapidly [7, 12, 13]. However, these factors have little relevance to the protection of young infants by Tdap immunization of pregnant women.

As demonstrated in this study in England and Wales, Tdap vaccination of pregnant women was 93% effective in preventing pertussis in infants <2 months of age. Based on data from 2 studies of serologic correlates of protection, efficacy data on DTaP vaccines presently used in the United States, and the type of Tdap vaccine used in the United Kingdom, I believe this level of efficacy is to be expected [14–18]. Munoz et al [19] studied the antibody values in 2-month-old infants whose mothers received a 5-component (pertussis toxoid [PT], filamentous hemagglutinin [FHA], pertactin [PRN], and fimbriae types 2 and 3 [FIM 2/3]) vaccine in pregnancy. They found the following enzyme-linked immunosorbent assay geometric mean antibody values in the sera from the infants: PT, 20.6 EU/mL; FHA, 99 EU/mL; PRN, 71.1 EU/mL; and FIM 2/3, 510.4 EU/mL.

Previous studies by our group in Germany [14] and Storsaeter et al [18] in Sweden showed that children who had received the 3-dose primary pertussis vaccine series and had serum antibody values to either PRN or FIM were protected >70% of the time for 20–24 months. Warfel et al [20] showed that infant baboons whose mothers had received a primary DTaP vaccine series and then a dose during pregnancy were protected against clinical illness, but not infection, when challenged with *Bordetella pertussis*.

Of the 2 Tdap vaccines available in the United States, one contains PT, FHA, PRN, and FIM 2/3 whereas the other contains PT, FHA, and PRN. In the United States, >50% of the currently circulating strains are PRN deficient [21]. Therefore, it is important to ask whether the infants of women given the 3-component Tdap vaccine during pregnancy will be protected during their first 2 months of life. The answer to this question is yes. Antibody to PT prevents all but mild illness in children, and a PT toxoid vaccine has been exclusively used in Denmark for 17 years and has controlled epidemic pertussis [22].

In young infants, severe disease and death is caused by PT and the extreme leukocytosis with lymphocytosis that it causes, and not by the toxin or toxins that cause paroxysmal cough and apnea [8, 23–25]. Antibody to the A subunit of PT in the serum of young infants born to pregnant women vaccinated during pregnancy will prevent severe leukocytosis with lymphocytosis in these infants [26].

Tdap vaccine administration has been shown to be safe in pregnant women [19, 27]. We now have the opportunity to prevent all pertussis deaths and severe disease in young infants. In the United States, we must find a way to remove obstacles to the universal use of Tdap vaccine in pregnant women. Unfortunately, financial barriers to Tdap administration by obstetricians in the United States will be difficult to overcome. However, until these barriers are addressed and remedied, young infants whose mothers are not vaccinated will continue to develop severe and fatal *B. pertussis* infections.

Notes

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The author has submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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