Early prevention of pertussis is key

In the conclusion of their interesting Article, Daan Barug and colleagues state that their data "support a start of pertussis vaccination at age 3 months instead of 2 months in the case of timely administration of maternal Tdap [tetanus, diphtheria, and acellular pertussis] vaccination".[1] Although this might be true for pertussis vaccination per se, unfortunately no stand-alone pertussis vaccine is broadly available.[2] In fact, in this study from the Netherlands, all infants received a diphtheria, tetanus, and pertussis-inactivated poliomyelitis-*Haemophilus influenzae* type b-hepatitis B six-in-one vaccine. Postponing the first dose from 2 months to 3 months might be disadvantageous for optimal protection against diseases other than pertussis—for example, invasive *Haemophilus influenzae* type b infection. Moreover, the measurable blunting of the immune response against pertussis vaccine antigens is not different when the immunisation series in infants whose mothers were immunised in pregnancy is delayed to age 3 months compared with age 2 months, as the authors themselves correctly point out by citing studies from the UK and Belgium.[3-5] Therefore, early protection against pertussis, diphtheria, tetanus, poliomyelitis, hepatitis B, and *Haemophilus influenzae* type b is still a valid option in the era of immunisation of pregnant women against pertussis.

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Authors' reply

We agree with Ulrich Heininger that when altering the primary infant vaccination schedule for the six-in-one diphtheria, tetanus, and pertussis-inactivated poliomyelitis-*Haemophilus influenzae* type b-hepatitis B (DTaP-IPV-Hib-HepB) vaccine from a dose at ages 2, 3, and 4 months to a reduced dose schedule (with doses at ages 3 and 5 months) in cases of timely maternal tetanus, diphtheria, and acellular pertussis (Tdap) vaccination during pregnancy in babies born full-term, one needs to take into account not only protection against pertussis[1] but also against the other diseases.

We investigated potential disadvantages of a reduced-dose schedule for optimal protection against diseases other than pertussis, particularly *Haemophilus influenzae* type b (Hib) infections. In the Netherlands, vaccination against Hib was introduced in 1993. From 1995–98, when a 3, 4, and 5 months primary vaccination schedule for DTaP-IPV-Hib was used, a mean of five Hib cases per year was observed in infants younger than 1 year. A mean of five Hib cases per year was also observed in the period after 1999, when a months 2, 3, and 4 schedule was used.[2] Only six cases of Hib were reported for infants aged between 2 months and 3 months in the period between 2010 and 2017. One must weigh the potential extra cases that can occur between 2 months and 3 months of age against the benefits of one fewer dose of DTaP-IPV-Hib-HepB for all children born full-term to mothers vaccinated during pregnancy and of the first vaccination occurring at an older age. Of course, invasive Hib cases should be closely monitored after this vaccination schedule switch. High vaccine effectiveness has been observed against confirmed invasive Hib disease, both following two and three primary doses.[3] There is no reason to believe that the effectiveness of the Hib vaccine will be lower after the schedule change.

We previously described higher antibody concentrations for most pneumococcal serotypes following a months 3 and 5 schedule compared with a months 2, 3, and 4 schedule for the 13-valent pneumococcal conjugate vaccine (PCV).[4] PCVs are given simultaneously with the DTaP-IPV-Hib-HepB combination vaccine. A later start of the first vaccination and a longer interval between vaccine doses improves priming and antibody concentrations, with less potential for interference from maternal antibodies.[5] We could not compare blunting after first vaccinations at age 3 months versus age 2 months but, if anything, we would expect less blunting with a first vaccination at an older age. Although we admit that early protection against pertussis, diphtheria, tetanus, poliomyelitis, hepatitis B, and Hib remains a valid option in the era of immunising pregnant women against pertussis, we favour a reduced-dose schedule with a later start when feasible.

We declare no competing interests.

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