Reply to Domenech de Cellès et al.: Infection and transmission of pertussis in the baboon model

We developed a nonhuman primate model to study whether pertussis vaccination is able to disrupt *Bordetella pertussis* colonization and transmission, and demonstrated that baboons vaccinated with the acellular pertussis vaccines (aP) were protected from classic pertussis symptoms (i.e., coughing and leukocytosis) but were highly colonized and transmitted pertussis to contacts in two of two experiments (1). In their letter to the editor, Domenech de Cellès et al. question our extrapolation of results from the baboon model to transmission in human populations (2). We agree that these data should not be directly extrapolated to pertussis transmission in humans. Although baboons are >96% genetically similar to humans, there are likely differences in how the species respond to vaccination and infection. We also agree that aP-vaccinated infected people are likely less efficient at transmitting pertussis compared with unvaccinated infected people, although it is not clear to what extent. In our model, the time required for transmission was greater when the infected baboon was aP-vaccinated compared with unvaccinated animals (3). However, in the baboon model, aP did not prevent infection as well as whole-cell vaccine (wP); therefore, it is reasonable to conclude that circulation of *B. pertussis* will be higher in an aP-vaccinated population than in a wP-vaccinated population.

We disagree with Domenech de Cellès et al.’s (2) implication that current epidemiological evidence argues against our findings. In the 2012 pertussis outbreak in Washington State, 75.8% of pertussis-infected patients aged 3 mo to 10 y were up-to-date on aP vaccinations, indicating that in humans, aP does not provide sterilizing immunity (4). Domenech de Cellès et al. present epidemiological data showing that the introduction of aP vaccine in Sweden in 1996 resulted in a dramatic decline in pertussis incidence following a 17-y lapse in pertussis vaccination. In figure 1A of ref. 2, Domenech de Cellès et al. highlight an 85% reduction in pertussis incidence “in infants too young to be vaccinated” and argue that this indicates aP indirectly protected unvaccinated infants by reduced circulation among vaccinees (i.e., herd immunity). However, the data presented includes all infants <1 y. Because >98% of the Swedish population is vaccinated with aP at 3, 5, and 12 mo, about 75% and 60% of infants <1 y would have received one or two aP doses, respectively (5). Nilsson et al. recently showed that pertussis incidence in 5- to 12-mo-old Swedish infants was reduced from 526 of 100,000 for unvaccinated infants to 95 of 100,000 and 24 of 100,000 for infants with one and two aP doses, respectively (5). Therefore, it is not clear to what extent the observed reduction in infant pertussis is attributable to herd immunity versus individual vaccine-induced immunity. One of the clear advantages of studying transmission in the baboon model is the ability to monitor *B. pertussis* colonization and symptoms over time, allowing for the unbiased detection of mild and asymptomatic pertussis. Although human clinical and epidemiological data are more directly relevant, that data rely on case definitions based on classic pertussis, leading to underdiagnosis of mild infections. Therefore, we feel it is wise to consider both human and animal data when studying the mechanisms underlying pertussis resurgence, while considering the caveats associated with each dataset.

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