In our study, vaccination with PCV before and/or after IPD was associated with lower IgG concentrations specifically against the infecting serotype, but responses to other vaccine serotypes were unaffected. As this phenomenon initially clustered around the period following the introduction of the 7-valent PCV and was particularly associated with serotype 6B, which was the most prevalent serotype in carriage at the time, we proposed that nasopharyngeal carriage before or at the time of PCV in infancy might have led to the serotype-specific unresponsiveness observed. This is in line with several clinical trials reporting an association between nasopharyngeal carriage before or at the time of vaccination with PPV or PCV in infants or toddlers and lower serotype-specific post-vaccination responses to the carried serotype [5–9]. It is also possible that pneumococcal infection itself could have contributed to the lower IgG concentrations against the infecting serotype. It has been proposed that the observed serotype-specific unresponsiveness is due to depletion of the memory B-cell pool after exposure to a large pneumococcal capsular polysaccharide load following carriage or disease [10]. The generation of suppressor T cells could be another possible but unlikely explanation because human studies have not identified pneumococcal serotype-specific T cells [11]. Similarly, other mechanisms such as functional T-cell deficiency may explain lower overall—but not individual serotype-specific—antibody responses after conjugate vaccination [12]. Thus, a genetic basis for the observed serotype-specific unresponsiveness against the infecting serotype in PCV-immunized children with IPD seems unlikely. However, we can only speculate on possible immunological and/or environmental factors. This clearly requires further study.

Note

Potential conflicts of interest. S. N. L. has performed contract research on behalf of St. George’s University of London and received assistance for attending conferences from vaccine manufacturers (outside the submitted work) but has not received any personal remuneration. M. P. E. S. has conducted contract research on behalf of Public Health England for vaccine manufacturers and has received personal fees from vaccine manufacturers as a speaker at international scientific meetings and as a member of advisory boards (outside the submitted work). R. B. has performed contract research on behalf of Public Health England for vaccine manufacturers (outside the submitted work). All other authors report no potential conflicts. All authors have 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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