Safaeian et al. (1) report two series of data that can be used to assess natural immunity following infection with human papillomavirus 16 (HPV16) and HPV18. First, inferences can be drawn from the fraction of women who are positive for HPV DNA (HPV DNA+) compared with the fraction who are negative for HPV DNA (HPV DNA−) but have a HPV-positive serology at study entry. Together with information on what fraction of women express a positive immune reaction after an HPV infection (about 60%) (2) and information about the mean duration of HPV infection (9–19 months for high-risk HPV) (3,4), the mean time from an HPV infection can be calculated for women who still have a detectable level of antibodies at enrollment as duration\_HPV\_DNA− × (HPV DNA+)/(HPV DNA−). The resulting lower bound of mean duration of detectable antibody reaction is 3.7–7.82 years for HPV16 and 10.34–21.82 years for HPV18. However, given the relatively young sample and the reported distribution of years since first sexual encounter [table 2 in (1)], these estimates are at the upper bound of plausible time limits since the infection for HPV16 and far beyond the limits for HPV18. For HPV16, this means that most women acquire their HPV infection shortly after their sexual debut and that antibody levels seem to be detectable for at least 6 years in those who show an initial antibody reaction, which indicates a very low waning rate. This also means that the effects of immune response with high antibody levels just after a very recent infection cannot be sufficiently evaluated in this study (5). In contrast, for HPV18, the estimated duration of a detectable immune response is too long when compared with the time since first sexual exposure to HPV. Although the prevalence of HPV18 DNA+ is in the expected range, the fraction of seropositive and HPV18 DNA− women is far too high, even higher than the fraction of seropositive and DNA− women for HPV16. A possible explanation for the large fraction of HPV18 seropositive and DNA− women in the Safaeian et al. study (1) is that, given the generally low immune response to HPV18, there may have been some false-positive findings among those classified as seropositive. Although the observed distribution of antibody titers at enrollment could also be a result of the waning of antibody levels, with the highest titers representing the most recent infections, the time frame from first sexual contact to accommodate an HPV infection, its clearance, and the waning of immunity is insufficient and suggests that the distribution of antibody titers reflects individual differences in immune response rather than waning.

A reasonable conclusion from the Safaeian et al. (1) study may be that although immune response persists for several years in a substantial fraction of women, immune protection exists only for the fraction of seropositive women with the highest titers. At the same time, the Safaeian et al. data (1) for HPV18 indicate a fraction of seropositive women that is too high, suggesting some false-positive findings. Still, the question of why HPV18 might be more affected by false-positive findings than HPV16 requires explanation.

RAFAEL T. MIKOLAJCZYK
JOHANNES HORN
OLIVER DAMM
ANDREAS M. KAUFMANN
MIRJAM E. E. KRETZSCHMAR

References