The public health implications of secondary measles vaccine failure

Mary Ramsay MB BS, MRCP, FFPH; Kevin Brown MD, MRCP, FRCPath

The occurrence of primary measles vaccine failure, where individuals fail to respond to their first dose of vaccine, is known to occur in around 5% of those vaccinated. This observation has led to the global policy for measles control recommending two doses of measles vaccination. Secondary vaccine failure, where individuals respond to vaccination but lose protective antibody over time, is less well quantified. Studying secondary failure is difficult, because it requires documentation of the initial response to vaccination and because confirmation of the diagnosis using standard serological assays is not straightforward. Despite this, secondary infection, as defined by a boost in IgG with high avidity IgG, in a patient with a history of previous infection or vaccination, has been associated with classical, mild atypical and even asymptomatic measles infection.1–4

The routine availability of RT-PCR (reverse transcription–polymerase chain reaction) to detect low levels of measles RNA, however, has made the confirmation of secondary infections more straightforward. The study by Mitchell and colleagues in this issue1 systematically compares disease severity in vaccinated and unvaccinated cases. This study confirms previous observations that the course of measles infection is less severe in vaccinated than unvaccinated cases. The high proportion of cases with documentation of two doses of vaccine and the absence of IgM positivity suggests that most of these cases were secondary failures. Although the authors make no attempt to estimate the frequency of secondary failure, it suggests that most countries with high coverage of vaccination should expect to observe such cases during measles outbreaks. Given the less severe presentation and the absence or low level of IgM in many cases, however, detection of such infections through routine surveillance requires the use of a less specific case definition and the availability of specialist microbiology, including measles RT-PCR and IgG antibody avidity.

The real public health question, however, is whether secondary infection from waning immunity could support measles transmission in highly vaccinated communities. As it is likely that unrecognised mild or unapparent secondary infections occur more frequently than observed in routine surveillance, secondary infection has potential to seriously impede global control strategies. No convincing evidence of secondary failures contributing to transmission has been published, and it has been hypothesised that high attack rates in vaccinees only occur under conditions of intense exposure.6 This would suggest that secondary infections may be less transmissible, as recently confirmed in a household study of mumps cases in the Netherlands.7 These conclusions would be consistent with the observation of sustained measles elimination in populations with high vaccination coverage, including those where many individuals were vaccinated more than 40 years earlier.

References