A(H1N1)pdm09 Vaccination of Healthcare Workers: Improved Immune Responses in Low Responders Following Revaccination

To the Editor—I read with great interest the article by Pathirana et al [1], which demonstrated that a 2-dose vaccination regimen with ASO3 adjuvant is needed to improve immune responses against 2009 pandemic influenza A virus subtype H1N1 (A[H1N1]pdm09) infection in low responders. The authors, in their discussion, suggested that the rapid induction of antibodies in the responders may have been due to a recall response to prior infection/vaccination. Indeed, that seems to be the case, although they did not elaborate on this in the results section. According to Figure 2A in their article [1], at the time of vaccination at least 10 of 25 subjects in the control (ie, responder) group had detectable and significant hemagglutination inhibition (HI) titers against A(H1N1)pdm09, which ranged from 8–64, while only 2 of 15 low responders had HI titers (8 in one low responder and 32 in the other). It would be interesting if the data from these 10 subjects were analyzed and shown separately, to allow assessment of
whether prior exposure influenced the overall responses of the group. Although it would be difficult to rule out that these subjects were exposed to A(H1N1)pdm09 prior to vaccination or that they were exposed to viruses that were similar to A(H1N1)pdm09, based on the available information on A(H1N1)pdm09 outbreak locally, the authors at least could rule out or rule out that possibility. It is also clear from these data that the kinetics of induction of HI titers were identical in both the low responder and control groups, peaking at day 14 after vaccination (Figure 2A), although the magnitude of responses was different. Hence, there was no rapid rise in antibody responses in the control group, compared with the low responder group.

I am intrigued by a lack of correlation between the magnitude of antibody response and the frequency of antibody-secreting cells (ASCs; Figure 2A and 2C and Figure 3A and 3C). The frequencies of ASCs among low responders and high responders ranged from 1 to 350 per 10^6 peripheral blood mononuclear cells after the first dose of vaccine, with corresponding HI titers ranging from 5 to 5120 (Figure 2A and 2C). However, in low responders, the frequencies of ASCs ranged from 5 to 7500 after the administration of a booster dose of vaccine, with HI titers ranging from 5 to 2560 (Figure 3A and 3C). It is not clear why, despite a 20-fold increase in ASCs, there was no corresponding increase in HI titer after booster receipt. Furthermore, the lack of correlation extended to antigen-specific antibody isotypes, as well (Figure 2B and Figure 3B). Could this have been due to a simple error of overestimating the ASC frequencies in Figure 3C by a factor of 10, or is there another explanation for this discrepancy?

It is well-known that not everyone responds well to vaccinations, and the lack of optimal responses to many vaccines in a small proportion of the recipients is documented. Several factors influence the immunogenicity of vaccines, including age; prior immune response to the antigen; structure, stability, and nature of the antigen; underlying medical conditions; chronic stress; and status of innate adaptive immune systems [2–4]. In the case of A(H1N1)pdm09 vaccine at least, the stability of hemagglutinin may be a contributing factor to the poor immunogenicity, because the low responders in this study had poor responses only to the A(H1N1)pdm09 vaccine component and not to the influenza A virus subtype H3N2 vaccine component [5]. Detailed studies taking a systems biology approach should provide clues as to why some individuals fail to mount optimal immune responses to vaccinations. Nevertheless, it is exciting to note that poor responses can be overcome with strategies such as revaccination, as was done in the present study, as well as in studies involving hepatitis B vaccines, those that explored alternate delivery routes, and those that investigated increased doses of the antigen [1, 6–9].

**Note**

**Potential conflicts of interest.** Author certifies no potential conflicts of interest.

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**References**


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