Letter to the Editor

“Original antigenic sin”: A potential threat beyond the development of booster vaccination against novel SARS-CoV-2 variants

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To the Editor—Recently, concern has increased over the emergence of novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) variants, which are spreading rapidly across the globe. These variants of concern (B.1.1.7, B.1.351, P.1, and B.1.427/429) have been initially reported in the United Kingdom, South Africa, Brazil, and California, respectively.¹ All existing immunity against related coronaviruses.¹⁰ The hypothesis of antigenic distance was proposed to explain how the efficacy of vaccines could be influenced by the difference or relatedness of prior vaccinations. This hypothesis is substantially evident in the case of dengue fever-related vaccine research. Once an individual is immunized against a dengue virus variant, the booster shot for the second variant is unlikely to be successful because it triggers only the original neutralizing antibodies rather than effective antibodies for the new variant.¹² This scenario also applied to the human papillomavirus Gardasil 9 vaccine. The vaccine contained 4 antigens presented in the original Gardasil in addition to 5 novel antigens. Individuals who had been vaccinated previously by original Gardasil exhibited lower levels of antibodies against 5 new antigens compared with those who had never been vaccinated for human papillomavirus.¹³

In the context of influenza infection, Choi et al¹⁴ noticed that following the vaccination program against the 2009 pandemic H1N1 influenza, individuals who had already been given a seasonal influenza virus vaccination developed lower antibody response than those who had never been vaccinated against influenza virus. Therefore, OAS can leave individuals with limited and imprinted memory immune response, and booster vaccination containing novel versions of the pathogen may not provide as much protection.

Given the cross-reactivity feature of antibodies against SARS-CoV-2 and other β-coronaviruses,¹⁰ the occurrence of OAS for initial and subsequent variants of SARS-CoV-2 would not be unexpected. On the other hand, when it comes to the incidence of ongoing mutations, booster immunization may become a necessary countermeasure for combating the novel resistant variants to current vaccines. If OAS is feasible in the case of SARS-CoV-2 and its emerging variants, the effectiveness of the booster dose will somehow be questioned. Clinical trial NCT04785144 is recruiting to assess the immunogenicity of the mRNA-1273.351 vaccine, which has recently manufactured for immunization toward the novel South African variant of SARS-CoV-2. To evaluate the efficacy of this booster dose on those who have received 2 vaccinations of mRNA-1273, the trial has been designed in 2 arms. The first arm evaluates the administration of a booster dose containing mRNA-1273.351 solely, whereas the

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The second arm contains both mRNA-1273.351 and mRNA-1273 in equal proportions. The consequences of this trial could shed light on how OAS may alter the effectiveness of booster vaccination for novel SARS-CoV-2 variants. Eventually, further well-designed animal or human studies on a different type of vaccines are required to evaluate the efficacy of booster immunization over the potential threat of OAS in SARS-CoV-2 vaccines.

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