TO THE EDITOR—I read with great interest the article by Marcelin et al [1] on the presence of preexisting antibodies against neuraminidase (NA) protein and their role in conferring protection against the pandemic H1N1 (pH1N1) virus. I am intrigued by their observation (Figure 1A, panel against A/Tennessee/1–560/2009) that individuals 60–64 years of age had the highest titers against pNA, even more than those observed among the older cohort. Although there appears to be no impact of vaccination on seroconversion rates among this group (Figure 1B, panel against TN), there is no corresponding increase in hemagglutination inhibition (HA) titers against pH1N1 virus (Figure 2A and B panels against TN). It is not clear whether this group had prior contact with the influenza virus of swine origin,
which would explain their high preexisting titers against pH1N1 NA, because the NA gene of pH1N1 virus belongs to the Eurasian swine lineage.

There is an increase in both anti-pNA and anti-pHA antibody titers with age that appears to increase following seasonal influenza vaccination (Figures 1 and 2). However, because there is variability in terms of anti-NA responses among different age groups, it is not clear whether this is reflective of the varying amounts of NA in the vaccines used, because the vaccines are quantified on the basis of HA content only [2]. It would have been more informative if the authors had provided the quantities of NA present in the vaccine preparations that were used in these clinical studies.

The presence of serum anti-NA antibodies in humans has been reported [3] and has been implicated in conferring resistance against influenza viruses in clinical studies [4]. In addition, influenza NA–based vaccines have been shown to be safe and immunogenic in humans [5] and have conferred varying degrees of protection against viral challenge in animal studies [6]. However, because the neuraminidase inhibition (NI) assay looks at the ability of serum antibodies to inhibit the conversion of the substrate by NA in a chemical reaction in vitro, they do not reflect the ability of these antibodies to reduce the viral titer. Given the limitations of the NI and enzyme-linked immunosorbent assays, I feel that analyses via antibody-dependent cell-mediated cytotoxicity and complement-mediated lysis after adsorption of sera against HA would provide an immunological effector mechanism for the protective role of NA-specific antibodies.

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