LETTER

The association of seasonal influenza vaccination and pandemic influenza A(H1N1) 2009 infection

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In 2010 Skowronski and colleagues reported that seasonal influenza vaccine appeared to increase the risk of pandemic influenza H1N1-2009 (pH1N1) infection in the first pandemic wave in Canada (1). They suggested a number of possible explanations for their unexpected finding: firstly, that the results were an artefact of selection bias or confounding; secondly, that the results were due to partial mediation through a biological mechanism; and thirdly, that the results were due to a direct immune mechanism, such as antibody dependent enhancement (1). Rosella and colleagues have investigated in detail the first of these explanations, and confirm that it is unlikely an unidentified confounder could have been responsible for the apparent increased risk of pH1N1 infection and seasonal vaccination (2).

This study (2) further strengthens the validity of the original study findings (1) and raises again possible explanations for those findings. While the plausibility of a direct immunological mechanism remains uncertain, there is other evidence that partial mediation could provide a reasonable explanation. Skowronski and colleagues suggested a biological mechanism which they referred to as “infection block”, where repeated vaccination blocks accumulated cross-protection to homosubtypic strains (1). The authors then argued that implausible parameters associated with vaccine coverage and influenza infection were needed for this mechanism to explain their observations (1).

As an alternative explanation for these findings, we have previously suggested a biological mechanism based on the concept of “temporary immunity”, a broad non-specific immunity that develops almost immediately after influenza virus infection.

Temporary immunity provides protection, initially almost complete, against infection with any other influenza virus, independent of type and sub-type (3). The duration of temporary immunity is modelled to be within the range of 3-6 months and, although its mechanism is not completely understood, it is likely to depend on a mixture of innate and adaptive immune responses (3).

Our hypothesis suggests that seasonal vaccination leads to a decrease in influenza infections in effectively vaccinated people, which leads to the absence of temporary immunity in those people, which in turn leads to an increased risk of pandemic infection. Using plausible input parameters in the context of seasonal influenza vaccination and influenza infection, we have further modelled temporary immunity to show that it could provide an explanation for an increase in the risk of seasonal vaccine and pH1N1 infection up to an OR of 1.8 if the majority of cases were children (4). The apparent increased OR was most evident for effective vaccine coverage (vaccine coverage multiplied by vaccine effectiveness) around 20-30% (4). This is consistent with the findings in the studies from Canada, where seasonal vaccine effectiveness was estimated as 56% (1) and vaccine coverage in Ontario in the first wave was 39% (2), giving effective vaccine coverage of 22%.

While the explanation remains uncertain for an observed increase in the risk of pH1N1 infection following seasonal vaccination, we suggest temporary immunity associated with seasonal influenza infection remains plausible. However temporary immunity cannot be described as a confounder because it is on the causal pathway (5). We thus agree with Rosella and colleagues that the apparent increased risk of pandemic influenza infection following seasonal influenza vaccination is unlikely to be explained by an unmeasured confounder.

References

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