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Health-care workers recovered from natural SARS-CoV-2 infection should be exempt from mandatory vaccination edicts

According to etymology, the word immune derives from the Latin immunis, which means exempt from public service, untaxed; unburdened. By extension, the term immunity means exempt from a particular infectious disease, but the term is now in danger of being equated with exemption from employment because of vaccine mandates that have been implemented or proposed in some countries. In the UK, unvaccinated health-care workers in England faced the prospect of imminent dismissal for representing a perceived danger to both themselves and to vulnerable patients, although the UK government is now consulting on whether the mandate should be scrapped. Many vaccine mandates include those who are naturally immune—which constitutes a large proportion of health-care workers in view of SARS-CoV-2 exposure in the workplace. However, there are compelling arguments against such unilateral mandates that bear repeating from the standpoint of accumulated knowledge around viral respiratory tract infections and immunity.

First, it is well established that for single stranded RNA viruses such as influenza, natural immunity after recovery from infection provides better protection than vaccination, which needs to be undertaken annually because of waning vaccine immunity.¹ The same has been shown for SARS-CoV-2; in one study, individuals exposed to natural infection were ten-times less likely to be reinfected compared with vaccinated individuals without natural infection (adjusted hazard ratio 0.02, 95% CI 0.01–0.04 for previous infection vs 0.26, 0.24-0.28 for vaccination). Individuals exposed to natural infection were also less likely to be admitted to hospital with COVID-19.²

Second, before the COVID-19 pandemic, it was a well-established principle that although systemic vaccination against viral respiratory tract pathogens protects vaccinees against serious infection, these individuals can still transmit virus to non-vaccinated individuals because of a lack of mucosal immunity.³ Therefore, individuals with immunity resulting from natural infection are probably less likely to transmit the infection to vulnerable patients (who should themselves be vaccinated) compared with those who are vaccinated but not naturally immune. Long-term immunity in the upper airway cannot be directly measured, and serum antibody levels are not a surrogate for mucosal immunity.

Third, numerous studies have shown that vaccination in individuals with previous natural SARS-CoV-2 infection induces so-called superimmunity (or hybrid immunity)ie, higher antibody and T-cell responses compared with vaccination alone.⁴ This concept is often evoked in favour of vaccination, but this super-immune state has no proven long-term clinical correlates, and an increasing number of studies show marginal, if any, additional benefits of vaccination in individuals with natural immunity. Attributing higher serum antibody responses in vaccinated individuals to superiority over natural infection is erroneous, as considerable time might have elapsed since the natural infection with the expected waning of antibody levels. Additionally, natural infection, with induction of strong interferondependent immunity in the upper airways, could lead to interferonrelated influenza-like symptoms, but with the innate cytokine response preventing sufficient breach of the mucosal barrier for clinically

significant antibody generation. Intramuscular vaccination will readily generate an antibody response, which is measurable as serum antibodies, albeit transiently. This phenomenon cannot be used to claim that vaccines are better than natural infection.

In some countries, including Germany, the voices of immunologists around the equivalence of natural immunity to vaccination are at least partly heard, since health-care workers who have recovered from natural SARS-CoV-2 infection are exempt from mandated vaccination for 90 days.⁵ However, based on the history of viral pneumonia and natural immunity, the scientific basis of this time frame is unclear—arguably it should be indefinite.¹

There is an ongoing shortage of health-care workers in England, which a vaccine mandate would probably exacerbate; indeed, this seems to be the primary factor in the UK government's reconsideration of the policy. A strong component of averting a further crisis in healthcare personnel should include making politicians aware of the power of natural immunity in individuals who have recovered from COVID-19.

I declare grants from Pfizer and Janssen, outside the submitted work.

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- 1 Krammer F. The human antibody response to influenza A virus infection and vaccination. Nat Rev Immunol 2019; **19:** 383–97.
- 2 Shreshta NK, Burke PC, Nowacki AS, Terpeluk P, Gordon SM. Necessity of COVID-19 vaccination in previously infected individuals. *Clin Inf Dis* 2022; published online Jan 13. https://doi.org/10.1093/cid/ciac022.
- 3 Connell AR, Connell J, Leahy TR, Hassan J. Mumps outbreaks in vaccinated populations—is it time to re-assess the clinical efficacy of vaccines? Front Immunol 2020; 11: 2089.
- 4 Crotty S. Hybrid Immunity. Science 2021; 372: 1392–93.
- 5 Robert Koch Institut. Fachliche Vorgaben des RKI für COVID-19-Genesenennachweise. https://www.rki.de/DE/Content/InfAZ/N/ Neuartiges_Coronavirus/ Genesenennachweis.html (accessed Feb 2, 2022).