Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

SARS-Cov-2 immune waning and reinfection in care-home settings

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The unprecedented, real-life pressures of the COVID-19 pandemic have shone a harsh spotlight onto long held assumptions from medical research, not least in the field of human immunology. Faced with this unprecedented global dataset of human infection and immunity, it has become crucial to appraise and reappraise assumptions about the nature and measures of protective immunity, durability of antiviral immunity, and changes in immunity across the life course. The learning curve has been steep. At the start of the pandemic, there were opposing arguments. Some emphasised building protective herd immunity following natural infection,[1] while others argued that immune subversion mechanisms of human coronaviruses (such as those that cause winter colds) make annual, rolling reinfection the norm,[2] and tolerance of natural exposure came at an unacceptably high risk with an infection of such high case fatality rate, especially in elderly people. Although it is clear that disease severity and lethality are strongly associated with age,[3] the specific immune correlates of differential susceptibility are hard to delineate, since most studies indicate nuanced deficiencies in B cell and T cell immunity across the life course.[4]

To investigate some of these questions, Anna Jeffery-Smith and colleagues[5] studied immunity and reinfection rates during the second infection wave (by the Alpha variant, B.1.1.7) in 692 residents and 933 staff in UK care homes. They report on the risk of reinfection during the 9 months following initial infections at the start of the pandemic, and on the erosion of protective headroom (that is, the level of neutralising antibody in a given individual above the cutoff for likely protection) through the well established drop in neutralising antibody titre when the immune system is confronted by a variant of concern carrying mutations in key spike epitopes.[6] Jeffery-Smith and colleagues[5] report findings broadly in line with other studies[7,8] that found a risk of reinfection of less than 5%, which was associated with low neutralising antibody titres. However, these data are specifically informative and reassuring on two counts. Firstly, in almost all participants, irrespective of age, protective immunity held up well across the 9 months of the study. Secondly, protection existed even in the face of a more immune-evasive variant of concern, and in elderly residents who were found to be no more susceptible than the younger care-home staff. The high granularity of the analysis, down to the level of actual neutralising antibody titres, is helpful with respect to benchmarking values for correlates of protection in a real-life setting.

Since this cohort recruitment ended, in early 2021, the story of the pandemic has moved on considerably. Additional variables to be taken into consideration include other variants of concern, Alpha to Delta, with Delta dominant in many regions and causing widespread breakthrough infection, even in those previously infected or vaccinated. Furthermore, many countries have vaccination programmes, using diverse vaccine platforms and often prioritising vaccination of elderly people. Although Jeffery-Smith and colleagues[5] considered immune-waning following first-wave natural infection, we now need to understand durability of protection in those who have received two vaccine doses, with or without previous infection. These are the datasets feeding into current policy debates about whether there is a need for booster doses, and about long-term vaccination strategy. This debate is proving to be difficult and finely balanced, with experts and policymakers coming to different conclusions on the durability of effective protection. This might be an area where immune modelling is trumped by real-life data. Serum antibody titres following vaccination, at least with the mRNA vaccines, might wane more rapidly than after natural infection. Antibody levels achieved can be somewhat lower in people older than 65 years and waning is more profound in this group than in younger individuals.[9] Functional confirmation of the importance of this waning derives from reports that[10] a third dose of any COVID-19 vaccine reduced breakthrough infections by a factor of 11.3 in vaccinated adults older than 60 years. As debate over additional vaccine doses continue, the case for prioritising effective levels of protective immunity in elderly people is compelling.[10]

RJB and DMA are members of the Global T cell Expert Consortium and have consulted for Oxford Immunotec.

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