Title

Enhanced antibody responses to first vaccine dose in previously SARS-CoV-2 infected individuals may render the booster dose unnecessary

Authors

Charlotte Manisty,[1,2]† Ashley D Otter,[3]† Thomas A Treibel,[1,2] Áine McKnight,[4] Daniel M Altmann,[5] Timothy Brooks,[3] Mahdad Noursadeghi,[6] Rosemary J Boyton,[7,8]* Amanda Semper,[3]‡ James C Moon,[1,2]‡

1 Institute of Cardiovascular Science, University College London, London, UK

2 Department of Cardiology, St Bartholomew's Hospital, Barts Health NHS Trust, London, UK

3 National Infection Service, Public Health England, Porton Down, UK

4 The Blizard Institute, Queen Mary University of London School of Medicine and Dentistry, London, UK

5 Department of Immunology and Inflammation, Imperial College London, London, UK

6 Division of Infection and Immunity, University College London, London, UK

7 Lung Division, Royal Brompton & Harefield NHS Foundation Trust, London, UK

8 Department of Infectious Disease, Imperial College London, London, UK

†These authors contributed equally

‡Joint senior authors

*Corresponding author

Prof Rosemary Boyton, PhD, FRCP, FHEA

Professor of Immunology and Respiratory Medicine

Adult Infectious Disease, Department of Infectious Disease, Faculty of Medicine,

Room 8N22, Commonwealth Building, Hammersmith Hospital Campus

Imperial College London, Du Cane Road, London W12 0NN, UK.

Email: r.boyton@imperial.ac.uk

Rapid vaccine-induced population immunity is a key global strategy to control COVID-19. Vaccination programmes must maximise early impact, particularly with accelerated spread of new variants.[1] Most vaccine platforms use a two-dose prime:boost approach to generate an immune response against the virus S1 spike protein, the titres of which correlate with functional virus neutralisation and increase with boosting.[2,3] To enable larger numbers of people to receive the first dose, delayed administration of the second dose has been advocated and implemented by some.[1] The impact of prior SARS-CoV-2 infection on the need for boosting is not known.

We reasoned that prior infection could be analogous to immune priming and as such, a first "prime" vaccine dose would effectively act as "boost", so a second dose would not be needed. To test this, we undertook a nested case-control analysis of 51 participants of COVIDsortium,[4,5] in an ongoing longitudinal observational study of healthcare workers who underwent weekly PCR and quantitative serology testing from the date of first UK lockdown for 16 weeks. 24/51 had prior laboratory-confirmed mild or asymptomatic SARS-CoV-2 infection (positive serology by anti-nucleocapsid and/or Roche anti-S (RBD) antibody), whereas 27 remained seronegative. A median of 12.5 time-points per participant permitted the identification of peak antibody levels in seropositives whilst avoiding false negatives. All participants then received first dose Pfizer/BioNTech mRNA vaccine[2,3] and were assayed at 22±2 days after the first vaccination dose. Among previously uninfected, seronegative individuals, anti-S levels after vaccination were comparable to peak anti-S levels following natural infection. Among those with prior SARS-CoV-2 infection, vaccination increased anti-S more than 140-fold from peak pre-vaccine levels (Figure). This increase appears to be at least an order of magnitude greater than reported after a conventional prime:boost vaccine strategy in the previously uninfected[3]

These data suggest that for individuals receiving vaccination (here Pfizer/BioNTech mRNA vaccine), a potential approach is to include serology testing at or before the time of first vaccination to prioritise use of booster doses. This could potentially accelerate vaccine roll-out without compromising vaccination efficacy. With increasing variants (UK, South Africa, Brazil), wider coverage without compromising vaccine induced immunity could help reduce variant emergence. Furthermore, reactogenicity after un-necessary boost risks an avoidable unwelcome increase in vaccine hesitancy. Our data provide a rationale for serology-based vaccine dosing to maximise coverage and impact.

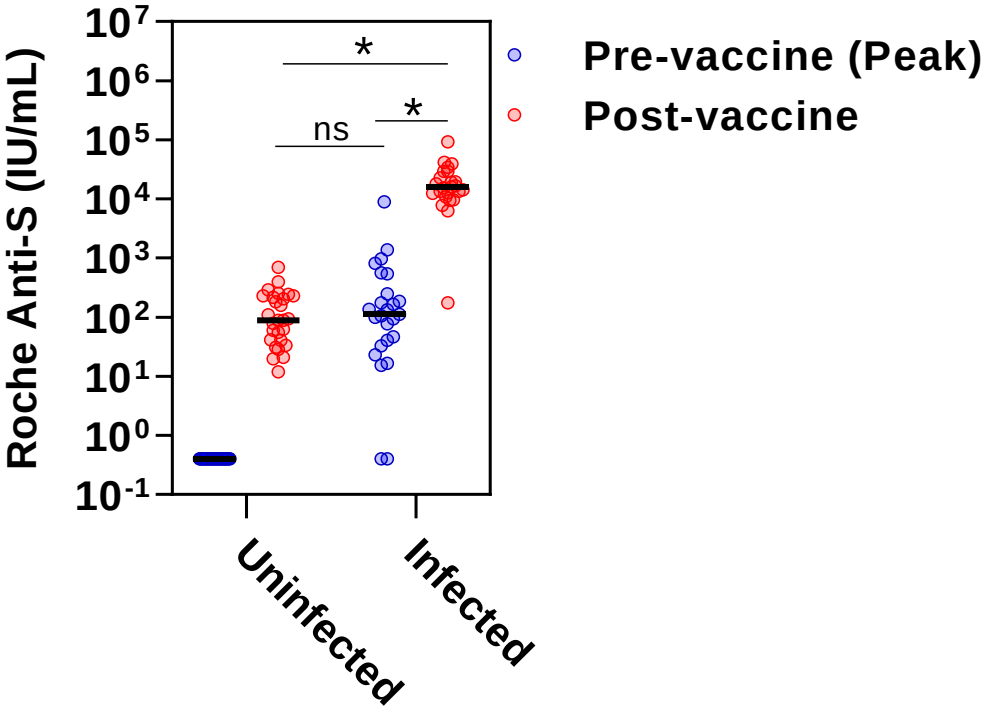

Figure. Comparison of serological response (Roche anti-S1 RBD) to a single dose of the Pfizer/BioNTech vaccine in individuals with and without laboratory evidence of prior SARS-CoV-2 infection.
51 participants (24 with prior laboratory confirmed SARS-CoV-2 infection) from a longitudinal, multi-timepoint COVID-19 healthcare worker study were sampled 22±2 days after a single dose of the Pfizer/BioNTech mRNA vaccine. Roche anti-S levels in those with no prior infection were similar to following mild SARS-CoV-2 infection. Anti-S levels among those with prior SARS-CoV-2 infection, showed anti-S levels more than 140-fold greater than at time of peak infection. *P<0.0001 for both

References:

1. https://www.gov.uk/government/publications/prioritising-the-first-covid-19-vaccine-dose-jcvi-statement/optimising-the-covid-19-vaccination-programme-for-maximum-short-term-impact. Accessed 29th January 2021

2. Polack FP, Thomas SJ, Kitchin N, et al. Safety and efficacy of the BNT162b2 mRNA Covid-19 vaccine. N Eng J Med 2020; 383:2603-15.

3. Walsh EE, Frenck RW, Falsey AR et al. Safety and Immunogenicity of Two RNA-Based Covid-19 Vaccine Candidates. N Engl J Med 2020; 383:2439-2450.

4. Treibel TA, Manisty C, Burton M, et al. COVID-19: PCR screening of asymptomatic health-care 476 workers at London hospital. Lancet 2020;395:1608-10.

5. Reynolds CJ, Swadling L, Gibbons JM. Discordant neutralizing antibody and T cell responses in asymptomatic and mild SARS-CoV-2 infection. Sci Immunol. 2020 Dec 23;5:eabf3698.

Funding:
Funding for the work presented in this Correspondence was donated by individuals, charitable Trusts, and corporations including Goldman Sachs, Citadel and Citadel Securities, The Guy Foundation, GW Pharmaceuticals, Kusuma Trust, and Jagclif Charitable Trust and enabled by Barts Charity with support from UCLH Charity. JCM and CM are directly and indirectly supported by the University College London Hospitals (UCLH) and Barts NIHR Biomedical Research Centres and through British Heart Foundation (BHF) Accelerator Award. MN is supported by the Wellcome Trust (207511/Z/17/Z) and by NIHR Biomedical Research Funding to UCL and UCLH. RJB/DMA are supported by UKRI/MRC Newton (MR/S019553/1, MR/R02622X/1 and MR/V036939/1), NIHR Imperial Biomedical Research Centre (BRC):ITMAT, Cystic Fibrosis Trust SRC, and Horizon 2020 Marie Curie Actions. ÁM is supported by Rosetrees Trust, The John Black Charitable Foundation, and Medical College of St Bartholomew's Hospital Trust. The authors thank the James Wigg Practice, London UK for support. The funders had no role in study design, data collection, or decision to publish this Correspondence.

Conflicts of Interest: DMA & RJB have consulted as members of GTEC (Global T cell Expert Consortium), Oxford Immunotec, UK

The corresponding author had full access to all data and had final responsibility for the decision to submit for publication.

Authors' contributions:
CHM - study design, data collection, funding, data analysis, interpretation, writing;
AO - sample analysis, interpretation, writing;
TAT - study design, data collection, funding, data analysis, interpretation, writing;
ÁM - study design, data collection, data analysis, interpretation, writing;
DMA - data analysis, interpretation, writing;
TB - data analysis, interpretation, writing;
MN - study design, analysis, interpretation, writing;
RJB - study conception and design, data collection, data analysis, interpretation, writing;
JCM - study design, data collection, funding, data analysis, interpretation, writing
AS - sample analysis, interpretation, writing.