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Persistence of IgG response to SARS-CoV-2

Little is known about the duration and protective capacity of the humoral immune response to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). In studies from Iceland[1] and the USA,[2] antibodies against SARS-CoV-2 did not decline within 4 months after diagnosis. However, other studies have reported rapid waning of antibodies within 3–4 months.[3–5]

Since April 22, 2020, we have been following up a representative cohort of 850 health-care workers from 17 Belgian hospitals. Participants are tested on a monthly basis for the presence of SARS-CoV-2 with quantitative RT-PCR (RT-qPCR) and for antibodies targeting S1 (spike subunit 1) protein with a commercial semi-quantitative ELISA (Euroimmun IgG; Medizinische Labordiagnostika, Lübeck, Germany), using a stringent manufacturer-defined cut-off for having a positive test result (ratio ≥1·1; NCT04373889).[6] By the end of September, 2020, seven rounds of testing had been done. To assess the longevity of the humoral immune response, we recorded the duration of the presence of detectable IgG in the serum of health-care workers who were seropositive for SARS-CoV-2. At least two consecutive positive samples were needed to classify a participant as seropositive, whereas disappearance of IgG was defined as having at least two negative tests after having been classified as seropositive. Only health-care workers who attended at least four testing points and had at least two positive tests were included in this assessment. Additionally, we did in-vitro neutralisation tests on IgG-positive samples, measuring the serum titre of antibodies needed to neutralise 50% of SARS-CoV-2 (NT_{50}).

By the end of September, 2020, 81 IgG-positive health-care workers had been identified. Of these individuals, five were asymptomatic, 75 had reported mild symptoms, and one needed hospitalisation. Median follow-up was 170 (range 62–199) days. In seven (9%) health-care workers, antibodies became undetectable after intervals ranging from 107 days to 159 days from presumed onset of infection (defined by day of positive RT-qPCR test or [if not available] day of onset of symptoms or [for asymptomatic patients] day of first positive serological test minus 14 days). Among 74 (91%) health-care workers who remained seropositive, median duration of antibody persistence (defined as the time between the day IgGs were last detected and the day of presumed onset of infection) is currently 168·5 (range 62–199) days. 71 (96%) of 74 health-care workers have already had antibodies for 90 days or more and 67 (91%) have had them for 120 days or more (appendix p 1).

Among the 74 seropositive health-care workers, 61 (82%) had neutralising antibodies in their most recent IgG-positive serum sample. Of note, of the 13 individuals with no detectable neutralising antibodies, eight had weak neutralising antibody titres (NT_{50} 55–100) and five had no measurable neutralising antibody titres from the start. Since antibodies specific for SARS-CoV-2 were only assessed for S1 protein, and because S1-specific cross-reactivity of prepandemic serum samples from patients infected with common cold human coronaviruses has been described,[7,8] an explanation could be that these five individuals are false-positive for SARS-CoV-2 antibodies. For as long as correlates of protection are not well defined, measuring anti-S1 IgG is an acceptable biomarker that probably slightly overestimates true seropositivity.

Follow-up of our cohort will continue at least until April, 2021. Based on data currently available, a rapid decline of SARS-CoV-2 IgG seropositivity or neutralising capacity has not been seen. It must be stressed that, compared with other studies, we used a stringent cut-off value for having a positive test result and a conservative definition for seroconversion. Our findings accord

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See **Online** for appendix

with earlier observations of antibody persistence after infection with severe acute respiratory syndrome coronavirus or Middle East respiratory syndrome coronavirus.[9] The importance of neutralising antibodies in long-term immunity against SARS-CoV-2 remains to be determined.

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