Figure 1 (facing page). Tumor-Mutation Profiles in the 2393 Study Patients.
Shown are tumor-mutation profiles according to race among men with primary prostate cancer (Panels A, C, and E) or metastatic prostate cancer (Panels B, D, and F). The data were obtained from targeted tumor-sequencing testing available to patients at the Memorial Sloan Kettering (MSK) Cancer Center (Integrated Mutation Profiling of Actionable Cancer Targets [IMPACT]) and from the Dana–Farber Cancer Institute (Oncopanel next-generation sequencing). (Details regarding testing methods are provided in the Supplementary Appendix.) Among the 2393 patients who were included in the study, 1484 patients had primary tumors, and 909 patients had metastatic tumors. The total mutation count in the two subgroups (Panels A and B) was calculated in the MSK-468 cohort (the largest subgroup in the study), in which patients were evaluated on a next-generation sequencing panel of 468 unique genes. Mutational frequency is shown for the genes that were most commonly altered in the study (Panels C and D). Actionable mutations are alterations that are the intended targets of precision-oncology drugs. Genes with actionable mutations (Panels E and F) include *ABL1*, *EGFR*, *ERBB2*, *BRAF*, *BRCA1/2*, *FGFR2/3*, *KIT*, *NTRK1/2/3*, *PDGFRA*, *RET*, *ROS1*, *ALK*, and *PIK3CA*. Among the patients with metastatic prostate cancer, genes with actionable mutations occurred more often in Black men than in White men (26.7% vs. 18.0%, P=0.05). DNA-repair genes include *ERCC5*, *MRE11*, *TP53BP1*, *POLE*, *RAD21*, *MSH2*, *MSH6*, *BRCA1/2*, *ATR*, and *ATM*. Mutations in DNA-repair genes occurred more often in Black men than in White men (22.5% vs. 15.6%, P=0.05) among those with metastatic disease.

men with metastatic prostate cancer were more likely than either White or Asian men to have tumor mutations in *AR*, along with mutations in DNA-repair genes and actionable genetic mutations. This finding could have implications for prognosis, response to therapy, and enrollment of minority populations in clinical trials and precision oncology studies.[3,5] Our study was limited by its use of confidence intervals that were not adjusted for multiple comparisons. To support and further explore the implications of these findings, we will need studies involving a larger number of non-White men for whom data are available regarding the effects of treatment and results from histopathological analysis on outcomes. The evaluation of such data could help to prevent a worsening of racial disparities in the diagnosis and treatment of prostate cancer.[3]

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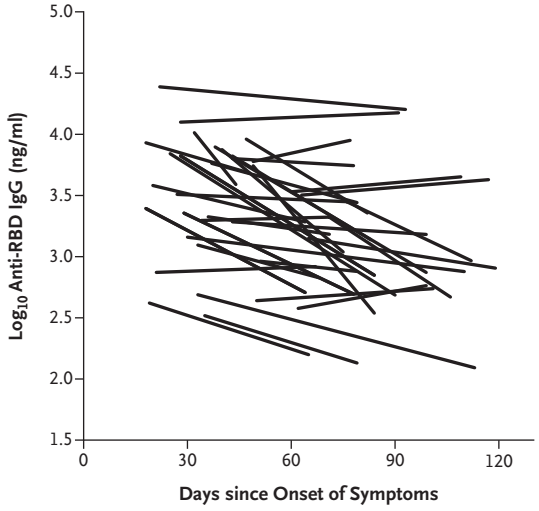
Rapid Decay of Anti–SARS-CoV-2 Antibodies in Persons with Mild Covid-19

TO THE EDITOR: A recent article suggested the rapid decay of anti–SARS-CoV-2 IgG in early infection,[1] but the rate was not described in detail. We evaluated persons who had recovered from Covid-19 and referred themselves to our institution for observational research. Written informed consent was obtained from all the participants, with approval by the institutional review board. Blood samples were analyzed by enzyme-linked immunosorbent assay (ELISA) to detect anti–SARS-CoV-2 spike receptor-binding domain IgG.[2] The ELISA was further modified to precisely quantify serum anti–receptor-binding domain activity in terms of equivalence to the

A



B

Predictor	Slope Estimate	Slope Standard Error	Slope 95% CI
Intercept	−0.0083	0.0016	−0.0115 to −0.0050
Age (per 10-yr change)	0.0026	0.0012	−0.0001 to 0.0051
Sex (female reference)	0.0010	0.0034	−0.0059 to 0.0079
First antibody level (log_{10} ng/ml)	−0.0049	0.0032	−0.0114 to 0.0016
Per 10 days since symptom onset	0.0016	0.0012	−0.0010 to 0.0041

Figure 1. Longitudinal Assessment of Anti–SARS-CoV-2 Receptor-Binding Domain IgG in Persons Who Recovered from Covid-19.

Approximately 80 persons who recovered from Covid-19 referred themselves to our institution to inquire about observational research. Of 68 persons who volunteered to provide initial blood samples, 41 returned to provide repeat samples. Of those persons, 3 were excluded from this analysis because of unclear timing of infection and 4 were excluded because of initial and repeat serum antibody measurements below the limit of reliable quantitative detection. For the 34 participants in our analysis, anti–SARS-CoV-2 receptor-binding domain (RBD) serum IgG concentrations were quantified by enzyme-linked immunosorbent assay as equivalent binding activity to a concentration of a control monoclonal IgG for at least two time points (31 of the 34 participants had two measurements, and the remaining 3 participants had three measurements). Panel A shows log-transformed IgG concentrations plotted against the time since the onset of symptoms in each participant. Panel B shows a linear regression model that was created to estimate the effects of the participants' age and sex, the days from symptom onset to the first measurement, and the first measured log_{10} antibody level on the slope reflecting the change in anti-RBD antibody levels (in log_{10} ng per milliliters per day). The values for age and antibody level were centered at the mean. The time since symptom onset was centered at day 18 and adjusted per 100 days. Thus, the intercept of the model can be interpreted as the average slope adjusted for age, sex, and time and value of the first measurement. CI denotes confidence interval.

concentration of a control anti–receptor-binding domain monoclonal IgG (CR3022, Creative Biolabs).

Infection had been confirmed by polymerase-chain-reaction assay in 30 of the 34 participants. The other 4 participants had had symptoms compatible with Covid-19 and had cohabitated with persons who were known to have Covid-19 but were not tested because of mild illness and the limited availability of testing. Most of the participants had mild illness; 2 received low-flow supplemental oxygen and leronlimab (a CCR5 antagonist), but they did not receive remdesivir. There were 20 women and 14 men. The mean age was 43 years (range, 21 to 68) (see the Supplementary Appendix, available with the full text of this letter at NEJM.org).

A total of 31 of the 34 participants had two serial measurements of IgG levels, and the remaining 3 participants had three serial measurements. The first measurement was obtained at a mean of 37 days after the onset of symptoms (range, 18 to 65), and the last measurement was obtained at a mean of 86 days after the onset of symptoms (range, 44 to 119).

The initial mean IgG level was 3.48 log_{10} ng per milliliter (range, 2.52 to 4.41). On the basis of a linear regression model that included the participants' age and sex, the days from symptom onset to the first measurement, and the first log_{10} antibody level, the estimated mean change (slope) was −0.0083 log_{10} ng per milliliter per day (range, −0.0352 to 0.0062), which corresponds to a half-life of approximately 36 days over the observation period (Fig. 1A). The 95% confidence interval for the slope was −0.0115 to −0.0050 log_{10} ng per milliliter per day (half-life, 26 to 60 days) (Fig. 1B).

The protective role of antibodies against SARS-CoV-2 is unknown, but these antibodies are usually a reasonable correlate of antiviral immunity, and anti–receptor-binding domain antibody levels correspond to plasma viral neutralizing activity. Given that early antibody decay after acute viral antigenic exposure is approximately exponential,[3] we found antibody loss that was quicker than that reported for SARS-CoV-1,[4,5] and our findings were more consistent with those of Long et al.[1] Our findings raise concern that humoral immunity against SARS-CoV-2 may not be long lasting in persons with mild illness, who compose the majority of persons with Covid-19. It is difficult to extrapolate beyond our observation period of approximately 90 days because it is likely that the decay will decelerate.[3] Still, the results call for caution regarding antibody-based "immunity passports," herd immunity, and perhaps vaccine durability, especially

in light of short-lived immunity against common human coronaviruses. Further studies will be needed to define a quantitative protection threshold and rate of decline of antiviral antibodies beyond 90 days.

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Hydroxychloroquine as Postexposure Prophylaxis for Covid-19

TO THE EDITOR: The window for postexposure prophylaxis against Covid-19 is narrow.[1-3] Therapy that is initiated up to 4 days after exposure to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is early treatment, not postexposure prophylaxis. The trial described in the article by Boulware et al. (published online on June 3 at NEJM.org)[4] was therefore largely about the prevention of symptoms in persons who may already have been infected. The trial was designed to detect a 50% relative reduction in new cases of symptomatic Covid-19; this estimate was overly optimistic. The trial was not powered to detect an important, but lesser reduction. Regardless, the authors found a nonsignificant (P=0.35) absolute difference of –2.4 percentage points (a 17% relative reduction) in the incidence of new symptomatic illness compatible with Covid-19 between the percentage of participants who received hydroxychloroquine within 4 days after exposure and those who received placebo. The upper boundary of the 95% confidence interval was an absolute reduction of approximately 7 percentage points (a relative reduction of approximately 50%), which was the investigators' prespecified target effect size.

We can draw three conclusions. First, hydroxychloroquine might be effective in early treatment, since the absence of evidence is not evidence of absence. Second, a larger trial involving participants with a virologic diagnosis should be conducted to detect a meaningful early treatment effect (e.g., a trial involving 8000 participants could detect a reduction in the incidence of symptomatic Covid-19 from 15.0% to 12.5%). Third, other trials examining preexposure prophylaxis and early postexposure prophylaxis should be considered.

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