Clinical pathology selected abstracts

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Clinical and immunological assessment of asymptomatic SARS-CoV-2 infections

September 2020—The clinical features and immune responses of people infected with SARS-CoV-2 who are asymptomatic are under investigation since people without disease symptoms can unknowingly spread the virus. As of Aug. 3, there were 17,965,128 confirmed COVID-19 cases worldwide, 4,749,138 of which were in the United States. The majority of those with SARS-CoV-2 infection have mild to severe respiratory illness with fever, cough, and shortness of breath, which appears two to 14 days after exposure. The authors conducted a study in which they described the epidemiological and clinical characteristics, viral levels, and immune responses in 37 asymptomatic people to better understand the clinical features and immune responses of people who are infected with SARS-CoV-2 and asymptomatic. The 37 asymptomatic people, all in the Wanzhou district of China, were diagnosed with RT-PCR–confirmed SARS-CoV-2 infections but had no relevant clinical symptoms in the preceding 14 days or while quarantined at the government-designated hospital for centralized isolation in Wanzhou. The authors showed that the median duration of viral shedding in the asymptomatic group was 19 days, and the asymptomatic group had a longer duration of shedding than the symptomatic group. In addition, the virus-specific IgG levels in the asymptomatic group were significantly lower than in the symptomatic group in the acute phase. Of interest, 40 percent of asymptomatic patients became seronegative and 12.9 percent of symptomatic patients became negative for IgG in the early convalescent phase, which was eight weeks after discharge from the hospital. The asymptomatic patients also had lower levels of anti-inflammatory cytokines. The authors concluded that these results show a reduction in IgG and neutralizing antibody levels in the early convalescent phase of COVID-19 and may have important implications in helping to understand "shield immunity" with this virus. They observed that IgG levels and neutralizing antibodies start to decrease within two to three months of infection. This makes it more challenging to rely on immunity passports. These data may support continuing to prolong public health interventions, including social distancing, hygiene, isolation of high-risk groups, and widespread testing. The authors suggest that additional serological studies are urgently needed to profile a greater number of symptomatic and asymptomatic people to understand the duration of antibody immunity and further study the infection rate.

Long Q-X, Tang X-J, Shi Q-L, et al. Clinical and immunological assessment of asymptomatic SARS-CoV-2 infections. *Nat Med.* 2020. https://doi.org/10.1038/S41591-020-0965-6.

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Anti-SARS-CoV-2 antibody decline in persons who experienced mild COVID-19

There is much interest in studying protective immunity to SARS-CoV-2 infection and identifying people who have recently recovered from COVID-19 to determine the role of anti-SARS-CoV-2 antibodies. An article published in *Nature Medicine* (see abstract above) examined the clinical and immunological features of asymptomatic SARS-CoV-2 infections. It suggested that anti-SARS-CoV-2 antibodies decay rapidly and that those who are asymptomatic have a weaker immune response to SARS-CoV-2 infection. However, the article did not describe the rate of antibody decline in detail. The authors of the study discussed herein conducted observational research to evaluate people who have recovered from COVID-19 and performed serial measurements of IgG anti-SARS-CoV-2 levels. They tested 34 study participants for anti-SARS-CoV-2 receptor-binding domain (RBD) serum IgG concentrations using an ELISA for at least two time points. (Three of the participants had three IgG measurements.) Infection had been confirmed in 30 of the 34 participants, and the remaining four had symptoms that were compatible with COVID-19 and had cohabitated with people known to have the disease, but they were not tested because of mild

illness combined with limited availability of testing. None of the participants received remdesivir. The study consisted of 20 women and 14 men who were a mean age of 43 years. The first IgG measurement was conducted a mean of 37 days after onset of symptoms (range, 18 to 65 days), and the last measurement was collected a mean of 86 days after onset of symptoms (range, 44 to 119 days). The results showed an initial mean IgG level of 3.48 $\log_{10}$ ng/mL (range, 2.52–4.41). The estimated mean change using a regression analysis model was − 0.0083 $\log_{10}$ ng/mL per day (range, − 0.0352–0.0062), which correlates with a half-life of approximately 36 days over the observation period. The anti-SARS-CoV-2 RBD antibody levels correlate with plasma viral neutralizing activity and are thought to be a predictive indicator for antiviral immunity. The authors found that early antibody decay was exponential after acute viral exposure. This loss of antibodies was faster than what was reported for SARS-CoV-1 and raises concerns about lasting humoral immunity against SARS-CoV-2 in people with mild illness. Because the majority of people with COVID-19 have mild illness, these results call into question the idea of herd immunity, antibody-based immunity passports, and, perhaps, vaccine durability. The authors noted that additional studies are needed to define a quantitative antibody-protection threshold and rate of decline beyond 90 days.

Ibarrondo FJ, Fulcher JA, Goodman-Meza D, et al. Rapid decay of anti-SARS-CoV-2 antibodies in persons with mild Covid-19 [correspondence]. *N Engl J Med*. 2020. https://doi.org/10.1056/NEJMc2025179.

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