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Commentary

Antibody responses in mild COVID-19 hospital staff

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Coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome (SARS-CoV-2) represents a major healthcare challenge threatening global public health, social stability, and economic development. One of the most striking aspects of COVID-19 is the stark and poorly explained differences in experiences of the disease, as some people never develop symptoms whereas others, sometimes apparently healthy, suffer from severe or fatal pneumonia. Manifestations of COVID-19, in fact, include asymptomatic carriers, patients with mild symptoms and fulminant disease characterized by sepsis and acute respiratory failure [1]. The host defense against SARS-CoV-2 and immune response, especially adaptive immune responses to the infection, represent key issues for a better understanding of the pathophysiology of the disease and an appropriate treatment. Antibodies to SARS-CoV-2 evolve rapidly after infection and should be used to better understand the antibody responses mounted upon virus infection and vaccination [2]. However, up to now, it is unclear whether there is difference in the antibody response found in individuals with severe, mild, and asymptomatic COVID-19, as most papers have been considered only hospitalized patients. It also remains unclear what degree and duration of immunity antibodies confer [3,4]. In this issue of *EBioMedicine,* Fafi-Fremer and colleagues describe the serological responses of 160 health care workers (physicians, nurses, hospital assistants, physioterapists, medical students and administrative staff) from Strasbourgh University Hospitals who recovered from reverse transcription polymerase chain reaction (rRT-PCR)-confirmed mild COVID-19 [5]. The paper deserves interest for many reasons. First, most published studies have focused on hospitalized patients with severe disease, whereas serological responses in patients with subclinical or mild infection have been poorly evaluated. Second, the Authors have investigated the kinetics of antibodies in a wide timeframe from 7 to 41 days after symptom onset, with a median time from onset of symptoms to blood collection of 24 days (IQR:21−28, range 13−39). Third, they have evaluated two different assays, a rapid lateral flow point-of-care test (POCT) for the detection of IgM and IgG against the SARS-CoV-2 receptor binding domain of the spike protein, and a flow-cytometry based assay which measures antibodies binding to the spike protein expressed at the surface of 293T cells (S-Flow assay). This assay allows to calculate two parameters: a) the percentage of cells having captured antibodies, defining the seropositivity; b) a quantitative measurement of the amount of antibodies and their efficacy. Finally, samples were tested for neutralization activity, using the pseudovirus neutralization assay. Neutralizing activities >50% and >80% corresponded to inhibitory dilution 50% (ID50) >100 and ID80>100, respectively.

Across all 160 participants, 159 (99.4%) had detectable antibodies by S-Flow, with 100% sensitivity achieved 21 days after symptom onset, thus confirming previously reported data on antibody kinetics [6]. The sensitivity of the rapid test, when combining either IgG or IgM positivity was 95.6%, whereas the positivity of IgM and IgG alone resulted 88.1% and 71.2%, respectively. It should be highlighted that other immunoassays reported a sensitivity higher for IgG than IgM [6,7]. The proportion of individuals with a neutralizing activity detectable at a 1:100 dilution of serum increased over time parallelling the increase of antibody titers observed with the S-Flow: it was 91.6% at 21−27 days and 97.9% >28 days after symptom onset. High neutralizing activity was observed in patients suffering from dry cough, high body mass index and high blood pressure. The presence of neutralizing antibodies have been associated with protective immunity to SARS-CoV-2 infection as passive immunotherapy based on transfer of antibodies from recovered COVID-19 (convalescent sera) decreased disease severity. However, many of these types of studies do not have control arms and the results of a recent randomized clinical trial suggest that the balance between efficacy and possible adverse events is still uncertain [8]. In animal models of COVID-19, the induction of neutralizing antibodies via immunization attenuated disease [9]. However, antibodies drive myriad of functions that both directly and indirectly interrupt infection. In addition to direct neutralization, antibodies may provide antiviral protection of the host via the recruitment of complement and/or Fc receptor, and a full appreciation of both neutralizing and extra-neutralizing antibody functions is needed for a rational design of effective vaccines and therapeutics.

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The paper of Fafi-Fremer and Colleagues, therefore, should be welcome because it provides new insights on the immune response to SARS-CoV-2 infection in patients who develop mild COVID-19, and highlights the value of serology assays to detect seroconversion in almost all patients. In addition, it presents data to inform on antibody functionality which are very useful to answer important scientific questions about immune protection from reinfection and to support research and development in vaccine trials. However, additional longitudinal studies profiling a more representative number of symptomatic and asymptomatic individuals are needed to better characterize the antibody response and to evaluate the persistence of antibodies upon SARS-CoV-2 infection. Finally, the role of both B and T cells in immune-mediated protection to viral infection deserves further evaluation as CD4+ cell responses to spike protein were found to be robust and correlated with the magnitude of the anti-SARS-CoV-2 IgG and IgA titers [10].

Declaration of Competing Interest

No conflict of interest to be declared.

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