Neutralizing Antibodies Against SARS-CoV-2—Important Questions, Unclear Answers

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As clinicians struggling to care for patients with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, we most want to read reports on randomized clinical trials of promising treatments or vaccines. However, descriptive epidemiologic studies can help us to develop those interventions.

In that spirit, I found the description of the development of neutralizing antibodies among patients with mild SARS-CoV-2 infection in China in this issue of *JAMA Internal Medicine* of interest.¹ The authors describe substantial variability in the development of these antibodies. To the extent that these antibodies help patients to recover or protect against infection, it is important to understand why some patients develop a stronger antibody response than other patients. In this study, higher antibody levels were seen in men, older patients, and those with indicators of stronger immunologic response, as well as older persons; however, men, older patients, and those with stronger inflammatory response and older age have generally fared worse, suggesting that the higher titers of antibodies do not necessarily lead to higher recovery rate. As this study looked only at patients with mild disease who survived, it could not correlate antibody levels with prognosis, and so we do not know whether certain groups need higher antibody levels to overcome the illness. Equally unclear is whether higher levels of antibody production, generally seen as an intermediary indicator of vaccine success, will result in greater protection against the virus. In this study, 10 of 175 patients had undetectable antibody levels despite documented infection. Are these patients susceptible to future infection, or do they have protection based on their infection sensitizing killer T cells or memory B cells? Answers to these pointed questions can lead to better protection when faced with this still largely unknown adversary.

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