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Editorial

The COVID-19 second wave: A perspective to be explored



As expected by many, we are now observing an increase of COVID-19 cases in many places where the epidemic first emerged. Among the most affected countries in Europe, Italy, France, United Kingdom, Germany, and Spain experienced an initial outbreak in the number of cases around March 2020 followed by a profound decay in the number of cases after May 2020, peaking again in November 2020. Russia had its first wave in the epidemic in May 2020, and after a valley in the number of cases, it is experiencing a new increase in the number of cases in November 2020 [<https://coronavirus.jhu.edu/data/new-cases>]. The new peaks of COVID-19 confirmed cases are accompanied also by an increase in the number of deaths, suggesting that the new wave does not reflect better diagnostic strategies and/or increased resources only. Larger heterogeneous countries like the United States and Brazil, which globally lead the number of COVID-19 related deaths, seems to experience a mix between the still ongoing first wave and a probably second wave in certain local geographic regions.

One new feature of this new wave in the COVID-19 pandemic is the affected population age group. According to the European CDC, the mean age of infected individuals and hospitalization are lower in this second wave compared to January-May. One can hypothesize that older individuals are less exposed at this time and therefore still less affected by this new epidemic wave. On the other hand, it is particularly the fact that in the first wave of the disease, younger individuals were not found to be symptomatic as they seem to be now, and the new situation could be considered unexpected.

SARS-COV-2 has a large spectrum of disease and symptoms. It has been recognized that most infections are asymptomatic or oligosymptomatic. The severity of the disease is in general associated to underline health conditions, sex, and age. It is also known that although effective, the regular and neutralizing antibodies may decay fast,¹ enabling hosts to be reinfected by the same coronavirus in a short period of time. Although hard to document, reinfection by SARS-COV-2 may occur, with some anecdotal reports being published. The first confirmed case of SARS-COV-2 reinfection

resulted in a less symptomatic infection in comparison to the first episode of infection,² but subsequent reinfection cases may result in a more severe second infection.^{3,4} In fact, when trying to develop a vaccine for severe acute respiratory syndrome and Middle East respiratory syndrome, it has been detected a phenomenon named antibody-dependent enhancement, which makes the response to the infection a more symptomatic disease.⁵ Therefore, it is conceivable that the new second wave of COVID-19 infections may represent many reinfection cases. The rationale for that would be that many younger individuals were infected during the first wave of the disease being misdiagnosed since the first infection was asymptomatic or oligosymptomatic. As specific immunity waned or the virus evolved leading to antigenic drift, these exposed younger individuals might act as a new susceptible population to reload the epidemic, being the second infection more symptomatic or severe. Immune response to SARS-COV-2, including antibody production or cellular immune response is heterogeneous which may make it difficult to use serologic tests for seroprevalence studies. Although the duration of viral shedding may be higher among asymptomatic individuals, up to 40% of asymptomatic individuals will never produce IgG compared to 12.9% of symptomatic cases.¹ The decay of regular IgG or neutralizing antibodies is fast in both symptomatic and asymptomatic persons.¹ It is conceivable that some infected individuals will not develop protecting immunity or will need multiple infections to develop protection.

This possibility should not be hard to explore. Up to now, the negative predicted value of serologic tests is low, especially among asymptomatic individuals who will not produce antibodies in as many as 40% of the cases.¹ The window period for SARS-COV-2 IgG production is of 6-12 days,⁶ and IgG will not last long among asymptomatic patients with a half-life of approximately 36 days.⁷ In this sense, should be interesting to test these individuals with acute disease using also an antibody-based assay since the reexposure to the antigen could boost the past antibody response bringing back an old and more mature breath of IgG. Perhaps, the confirmation of past infection could be done by using antibody avidity

tests in the positive samples. Antibody avidity refers to the strength with which an antibody binds to its related antigen.⁸ Low-avidity antibody is usually produced during recent infection, whereas the avidity of an antibody increases over time with the maturation of the IgG antibody response.⁹ IgG avidity assays have been used in the past to differentiate current from past infections with other viruses.^{10–12} Such knowledge could help understanding the current status and predict the future of this new pandemic.

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Ricardo Sobhie Diaz ^{a,*}, Tania Regina Constant Vergara^b
^a Federal University of Sao Paulo, Paulista School of Medicine, Infectious Diseases Division, SP, Brazil
^b Federal University of São Paulo, SP, Brazil

* Corresponding author.

E-mail address: rsdiaz@catg.com.br (R.S. Diaz).

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