

Update on the management of SARS-CoV-2 infection

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Comprehensive serological strategy for the diagnosis and monitoring of SARS-CoV-2. From infection to vaccine control

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ABSTRACT

SARS-CoV-2 serology is useful to identify past COVID-19 cases, and it is not useful for acute infection. Levels of specific SARS-CoV-2 anti-N and especially anti-S are expected to be maintained for long periods. At this moment there is not a clear correlate of protection after COVID-19 or vaccination, therefore serological follow up is not indicated in most cases.

Keywords: SARS-CoV-2, COVID-19, Serology, Vaccines

After SARS-CoV-2 infection, most individuals develop a specific antibody response that it is detectable from the first week post-symptoms, being 13 days the median time for IgM or IgG seroconversion [1]. Titres of IgG against SARS-CoV-2 spike (S) protein, correlate with neutralizing activity indicating a potential use of S protein as a vaccine immunogen [2]. Initially some reports found a declining trend of antibodies and neutralizing response during early convalescent period [3-5] although subsequent studies, and our own experience, have shown sustained humoral response, long-term B-cell memory and evidence of affinity maturation beyond the viral replicative phase in the respiratory tract [6-8].

Nevertheless, there is a great heterogeneity in the serological response of different individuals after natural infection by SARS-CoV-2. Early on in the pandemic numerous reports disclosed a rapid decay of the antibody levels [4,5]. Several factors could have been contributed to the initial impression that the immune response to SARS-CoV-2 was a very transient one, including short periods of follow up and technical limitations of diagnostic tests specially those based in detecting anti-nucleoprotein (N) antibodies [3]. More prolonged follow up shows a sustained response in most of the individuals. Anti-S IgM is

in many cases transiently expressed during the first months but still can be detectable in over 32% of infected individual by month 7 after recovery, further questioning the diagnostic value of IgM as an acute infection marker of COVID-19 [9]. It has been recently shown that affinity maturation occurs far beyond the replicative phase of SARS-CoV-2 in the airway epithelium, a process that increases the affinity of antibodies and remarkably the breath against variants [8]. In this respect it has been shown the presence of SARS-CoV-2 particles in the gut mucosa, a highly enriched ACE2 cellular milieu. Whether this gut mucosal infection can be the source of antigen presentation and affinity maturation occurs in regional follicular germinal centres and remains to be confirmed [6,8].

Overall, in cohorts of representative COVID-19 cases, a sustained humoral response is present in most of the convalescent individuals up to 12 mpi and data from the analysis of B-memory cells indicate that a considerable number of cells able to activate and produce anti-SARS-CoV-2 antibodies are long term maintained [6].

The immune correlates of protection upon SARS-CoV-2 infection or vaccination are so far unknown, however the levels and the stability of the anti-S specific antibodies and neutralizing response observed, together with the presumptive innate and cellular response capabilities developed, indicate that probably convalescent individuals are protected from systemic disease for long periods. In most of the studies it has been analysed the presence of antibodies in serum and the correspondence with those in respiratory mucosa, that can be more related to susceptibility for infection and transmission, is not clear. This is an issue of the highest relevance that warrants further research. Finally, this sustained immune response needs to be tested against the new SARS-CoV-2 variants that have been described precisely in areas with high attack rates and appear to be scape mutants under selective immunological pressure [10-13].

Vaccination is now in rapid deployment mainly in de-

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Table 1	SARS-CoV-2 Serologic markers after COVID-19, vaccination, or both.	
	Anti-N	Anti-S/RBD
COVID-19 convalescence	+/++	+/++
Vaccination (Spike: Pfizer/BNT, Moderna, AZ, Janssen)	-	++
COVID-19 and vaccination	+/++	+++

N: SARS-CoV-2 Nucleoprotein. S: SARS-CoV-2 Spike protein. RBD: SARS-CoV-2 Receptor Binding Domain of S protein.

veloped countries and this fact introduces a new complexity in serology interpretation. Main marker used in commercial test and results are described in Table 1. Natural infection by SARS-CoV-2 induces heterogeneous but maintained levels of antibodies against all viral components. So at this moment detection of anti-Nucleoprotein (N) is a hallmark of previous COVID-19 whereas after vaccination only anti-Spike (S) is detected. In convalescent individuals after vaccination there is a remarkable boost of production of anti-S antibodies and in this cases anti-N combines typically with very high levels of anti-S.

CONFLICTS OF INTEREST

The author declares no conflict of interests.

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