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1 How useful is serology for COVID-19?

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12 A paper in this journal, reports on the different sero-epidemiological studies carried out
13 around the world for SARS-CoV-2¹. This study helps to put into perspective the potential
14 interest of serology in SARS-CoV-2 infection. The first question was, according to
15 serological techniques, is it possible to identify positive serologies in patients sampled in
16 2019, before the epidemic? The answer is yes⁸. Depending on the different serological
17 techniques used, cross-reactions may be observed, particularly in children, which could
18 explain why SARS-CoV-2 is to date the only respiratory viral disease that does not affect
19 children^{2;3}. Indeed, in most cases, children are the most affected by respiratory viral
20 infections, this situation is reversed for SARS-CoV-2 for reasons that are not clear at this
21 time. The second major interest that these serological studies could have, would be to confirm
22 *a posteriori* that patients who were included in studies based on purely clinical criteria were
23 actually infected with SARS-CoV-2. Indeed, several studies, including the Recovery study in
24 England and that of Skipper et al.^{4;5}, have included in their evaluation patients who had not
25 been tested, or tested negative, at the time of inclusion. Performing serology retrospectively,
26 as in one recent study for example⁶, ensures that the patients included were indeed affected
27 with SARS-CoV-2. A recent study conducted in France, shows that the predictive value of the
28 clinical diagnosis of SARS-CoV-2 in patients who were subsequently serologically tested for
29 SARS-CoV-2 is less than 50%⁷. This means that studies in which there was no diagnostic test
30 to confirm the diagnosis included at least 50% of people who were not infected with SARS-
31 CoV-2. This also depends on the sensitivity of the serological test. This makes series without
32 a diagnostic test hard to interpret. Seroprevalence studies help to evaluate the extension of
33 epidemics. Incidences based on samples tested by PCR from one area to another have not
34 provided a complete epidemiological picture of the spread and lethality of the disease. In
35 Marseilles, we have systematically tested all symptomatic and non-symptomatic people since
36 February 2020⁸ and have tested 10% of the whole population. We were therefore able to

37 evaluate the percentage of positive people in the initial epidemic (incidence), at 8%. We had
38 also samples of peoples from three other regions in France: the Ile de France (which includes
39 Paris), the Grand Est, and the New Aquitaine regions. The incidence rates among patients
40 tested in these regions by PCR (unpublished data) surprisingly give a result exactly
41 superimposable to that of seroprevalence in the whole population of these areas, with 8% for
42 Marseille area (Etablissement Français du Sang, France, unpublished data), 10% for Ile de
43 France, 9% for Grand Est and 3% for Aquitaine³. The extent of population seroprevalence in a
44 region or country will provide a sense of the importance of social control measures such as
45 lockdown, the use of masks, or generalized testing. Moreover, it may allow clarifying the
46 lethality in our area independently of the qPCR testing capacity during the outbreak. In the
47 work carried out in this field, particularly in Italy⁹ and Spain¹⁰, it has been shown that
48 persons confined in house, when not tested for putative contagiousity, have more often been
49 positive than working unconfined persons. This is counter-intuitive, as the consequence that
50 SARS-CoV-2 carriers have not been detected. This raises the question of the value of the
51 lockdown of families when asymptomatic carriers are not detected. Seroprevalence is also a
52 very good evaluation of the prevention measures of the health care staff. In general, the
53 measurement of seroprevalence in Spain¹⁰ and Italy⁹ showed much higher prevalence of the
54 health care personnel, indicating a weakness in prevention measures as well as their high risk.
55 In Marseilles, the percentage of positive test results among health care staff in direct contact
56 remained very low in may 2020, at 3.5%¹¹, due to the importance of the protective measures
57 deployed. As a matter of fact, we had to import protective artefacts directly from China, as no
58 stock was available in France. All in all, this work opens the door to a more general reflection
59 on the conduct of epidemiological studies in order to refine the consequences of social or
60 protective measures in the spread of the virus in a given site.

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62 **Conflict of interest:** I declare that I have no competing interests

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64 **Ethical approval :** Not applicable

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