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Reinfection, recontamination and revaccination for SARS-CoV-2

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Abstract

The reports on COVID-19 describe the pandemic in waves. Similarly to the ocean's waves, the frequency and amplitude of the number of new cases and the number of deaths were globally quite regular, nevertheless, they showed important regional irregularities and actually the spreading direction has been generally rather unpredictable for COVID-19. One of the major reasons for the repeated outbreaks is the mutating capacity of the SARS-CoV-2 that allows the virus to infect persons who have natural immunity or have been vaccinated. Vaccination began in vast campaigns from the second year of the pandemic that was supposed to decrease the magnitude of the waves. Although it reduces the complications, the expected attenuation of the disease expansion has not yet been met. This paper gives a short overview of the most recent data on the rate of reinfection of vaccinated and non-vaccinated individuals. It points out that testing positive for a second time for SARS-CoV-2 does not necessarily mean a reinfection; it can also be interpreted as recontamination. The symptom free outcome as well as the rapid reconversion of the PCR test may help to make the difference between reinfection and recontamination. Awareness of this phenomenon may be valuable in times of human resource difficulties. The available evidence may suggest that the protective value of a prior infection could be better considered for the vaccine distributions in the future.

INTRODUCTION

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) infected more than 400 million people worldwide and caused the death of over 6 millions [1]. In the last two years SARS-CoV-2 became the most common cause of death from a single infectious pathogen, preceding mycobacterium tuberculosis, responsible for an estimated 1.4 million of victims in 2019 [2] and human immunodeficiency virus and malaria, the mortality of which went below 1 million in the last years [3].

Majority of the deceased people were retired Caucasians [1]. The geography of the disease expansion may explain why coronavirus, being the most devastating in North America and Europe, got outstanding media and political attention in comparison to other infections with high mortality even if these ones affect young people as much as the elderly. Reports directly showing patients with respiratory assistance faced many people for the first time with hospital intensive care. Beyond the statistical data these widely diffused images contributed to the shocking experience of the pandemic. COrona VIrus Disease 2019 (COVID-19) is the first epidemic in history that has been broadcasted in live from the beginning on.

There is no efficacious treatment for COVID-19. Hospitalisation may help in the oxygen supplementation and in the care of some complications of the disease. Vaccines of different types have been developed to yield protection from the infection. This occasion was a world premier for the mRNA vaccines [4, 5] and also the first adenovirus based vaccine authorized by the US Food and Drug Administration (FDA) [6]. To date their efficacy at the prevention of severe complications of COVID-19 is evident but their power to reduce the disease spread has not met the expectations [1].

Reinfection

The first reinfection by a different strain of SARS-CoV-2 was identified in the summer of 2020 with whole genome sequencing and comparative genome analysis in an immunocompetent person with an interval of 142 days between the two episodes [7]. In

this case the primary infection was symptomatic and the reinfection was asymptomatic. A larger analysis of several cases found that the reinfection may be either less severe, or may also have a more severe outcome as compared to the primary infection [8].

When the vaccinations started in spring 2021 the follow-up of the protective effect of recovering from a primary infection became problematic, since the promotion of the vaccination was so strong in the most affected countries, that the majority of the people got vaccinated. Nevertheless there are some publications that may help elucidate this issue.

No symptomatic reinfection was detected in 1265 British health care workers who had been followed with positive anti-spike-IgG for 31 wk [9]. In the national, federated database of Qatar there were 350.000 PCR-confirmed infections registered between 28th February 2020 and 28th April 2021. Among these cases 1300 reinfections were identified and these cases were matched with primary infections in a 1:5 ratio. The number of severe, critical and fatal cases were 158, 28 and 7 for the primary infections and 4, 0 and 0 for reinfections respectively. Vaccinated persons were excluded from the analysis. Severe outcome meant hospitalisation and critical outcome meant hospitalisation in intensive care unit [10].

These data support the hypothesis that recovering from a primary SARS-CoV-2 infection yields natural immunity that protects from both, the potential reinfection and the severe complications of a reinfection. However, vaccinations were declared to provide additional protection.

Breakthrough infections in vaccinated individuals and in those who had a prior infection were compared in the same Qatar database. The PCR cycle threshold is known to inversely correlate with viral load. Or, the cycle threshold value is 1.3 cycles higher for breakthrough infections following BNT162b2 vaccine, 3.2 cycles higher for breakthrough infections following mRNA-1273 vaccine, and 4.0 cycles higher for reinfections in unvaccinated individuals than at primary infection. Thus unvaccinated persons who recovered from a prior SARS-CoV-2 infection had the lowest viral load when getting a breakthrough infection as compared to mRNA vaccinated counterparts

[11]. In a cohort in Bangladesh including 1644 participants the naturally infected population was less likely to be reinfected by SARS-CoV-2 than the infection-naïve and vaccinated participants with one of the seven different vaccines authorised in this country [12]. A Danish study conducted among 3.800 blood donors who had SARS-CoV-2 PCR positivity found no evidence of decline in the proportion of detectable anti-SARS-CoV-2 antibodies over time up to 15 mo [13].

In contrast, in a study of 150.000 patients who had recovered from COVID-19 in Israel, those who were vaccinated had lower risk of reinfection than those who were not vaccinated. The difference is smaller in the elderly population. The paper does not report about the severity of the reinfections, The authors recognise that the lack of assessment of disease severity and hospitalisation is an important limitation of their work [14].

Recontamination

The second time contact with SARS-CoV-2 is not necessarily a second infection it may only be a contamination, which means that some pathogens get on a body surface or mucus membrane. Still, the invasion of the adjacent tissues does not follow, because the person's defence system prevents it.

Someone contaminated with SARS-CoV-2 is going to give a positive test, may possibly and transitionally transmit the virus but remains asymptomatic. However, the duration of the positivity of a contaminated individual following primary infection or vaccination will be presumably short. In our experience the duration of their positivity is around 5 days (unpublished data) as compared to the positivity of healthy individuals who undergo a first infection that is at least 8-20 days.

This is in reality what we may expect from the protective efficacy of vaccinations and natural immunity. They do not inhibit the viruses to reach the nasal mucosa when being in contact with an infected patient. Nevertheless, they assure a more reactive immunity that helps in preventing the development of the disease within the body.

The possible interpretations of a positive SARS-CoV-2 PCR test are summarised in Table1. Under the pressure of the pandemic it may be hard to accept that interpretation of the tests depend on the clinical situation, moreover if the clinical context is left out, decisions based exclusively on test results may be harmful. The importance of the correct interpretation of sustained PCR positivity at primary infection has been stressed, particularly in case of comorbidities needing rapid treatment such as certain malignancies [15]. The authorisation of asymptomatic health care workers to return to work has become the routine in many hospitals facing problems of human resources. Some other situations when a positive PCR test may be disturbing are listed in Table 2.

Revaccination

Initially, producers affirmed that two doses distanced with one month provide immunity for SARS-CoV-2. Except for Ad26.COV2-S from which one dose is equivalent with two doses of the other products. However, the level of protecting antibodies was found to decrease with time, so the potential necessity of a booster dose was discussed. It is important to note, that the waning of immunity was studied for vaccinated populations whereas for naturally immunised populations there are only observations of case series [16].

Currently, in most Western countries a booster is required 6 mo after the first vaccination for the official recognition of protection. The suggestion that the booster may or should be different from the primary vaccine adds to the confusion related to the efficacy of each single vaccine. We agree with the WHO's consideration that in view of the shortage of vaccines, assuring booster doses for some populations may rise the suspicion that other populations will miss even the primary vaccination [16].

In addition, the above mentioned results [11, 12, 13] show that natural immunity may even be stronger and last longer than the effect of vaccination depending on both the severity of the infection and the type of vaccination. The distribution of the vaccines dedicated to naturally immunised individuals rather to non-infected individuals would probably

have saved more lives and would certainly have been more equitable. This hypothetical redistribution would have concerned hundreds of millions of people.

Discussion

One of the destabilising lessons of the pandemics is that scientific predictions concerning the COVID-19′s clinical presentation and geographical expansion rarely proved correct.

Measures seeming reasonable at a point might turn out to be completely useless a couple of weeks later and vice versa. For instance, the nationwide testing in Slovakia in the winter of 2020 drew international attention and the identification of a high number of asymptomatic infections gained recognition. It was assumed that the containment of the detected individuals would prevent disease spread. Nevertheless, the country could not avoid the explosion of the disease and the overcharge of its healthcare system. Contrarily, Sweden was much criticised for the liberal management of the pandemic and had relatively high mortality rate in the first months, still many more restrictive countries had worse outcomes one year later [1].

Decision making and the observance of the prevalent decrees are even more unpredictable than the behaviour of the virus. Decision makers are challenged with opposing expectations but miss essential references. They have to solve dilemmas like the protection of the life of the elderly *vs* the job of the young or the equitable distribution of the vaccines *vs* the possibly most rapid care for their own population. On the other hand observance supposes explanations and never meant obedience.

With the arrival of the omicron strain some hope is shining that after more than two years the disease will pass in a more controllable phase.

CONCLUSION

Conclusions

1) Differentiation between recontamination and reinfection may be useful for persons tested positif with SARS-COV-2 PCR. 2) The protective effect of prior infection should be considered before vaccination against COVID-19. 3) Fairness should be respected in vaccine distribution at a global scale.

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