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Review

Actions and attitudes on the immunized patients against SARS-CoV-2

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ABSTRACT

The access to COVID vaccines by millions of human beings and their high level of protection against the disease, both in its mild and severe forms, together with a plausible decrease in the transmission of the infection from vaccinated patients, has prompted a series of questions from the members of the College of Physicians of Madrid (ICOMEM) and the society. The ICOMEM Scientific Committee on this subject has tried to answer these questions after discussion and consensus among its members. The main answers can be summarized as follows:

The occurrence of new SARS-CoV-2 infections in both vaccinated and previously infected patients is very low, in the observation time we already have. When breakthrough infections do occur, they are usually asymptomatic or mild and, purportedly, should have a lower capacity for transmission to other persons.

Vaccinated subjects who have contact with a SARS-CoV-2 infected patient can avoid quarantine as long as they are asymptomatic, although this decision depends on variables such as age, occupation, circulating variants, degree of contact and time since vaccination. In countries with a high proportion of the population vaccinated, it is already suggested that fully vaccinated persons could avoid the use of masks and social distancing in most circumstances.

Systematic use of diagnostic tests to assess the immune response or the degree of protection against reinfection after natural infection or vaccination is discouraged, since their practical consequences are not known at this time. The existing information precludes any precision regarding a possible need for future revaccination.

This Committee considers that when mass vaccination of health care workers and the general population is achieved, SARS-CoV-2 screening tests could be avoided at least in outpatient care and in the case of exploratory procedures that do not require hospitalization.

Keywords: COVID-19, viral variants, SARS-CoV2, vaccine escape, gap COVID-19, use of masks, COVID-19 screening, vaccines, follow-up of immunized persons.

Acciones y actitudes ante el paciente inmunizado contra el SARS-CoV-2

RESUMEN

El acceso a las vacunas frente a COVID-19 de millones de seres humanos y su alto nivel de protección frente a la enfermedad, tanto en sus formas leves como graves, junto a una verosímil disminución de la transmisión de la infección desde pacientes vacunados, ha motivado una serie de preguntas de los colegiados y de la sociedad. El Comité Científico del ICOMEM sobre esta materia ha tratado de responder a dichas preguntas tras discusión y consenso entre sus miembros. Las respuestas principales pueden resumirse así:

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La aparición de nuevas infecciones por SARS-CoV-2 tanto en vacunados como en previamente infectados, es muy escasa, en el tiempo de observación del que ya disponemos. Cuando ocurren infecciones de brecha, suelen ser asintomáticas o paucisintomáticas y, en principio, tendrían una menor capacidad de trasmisión a otras personas.

Los sujetos vacunados que tienen contacto con un paciente infectado por SARS-CoV-2 pueden evitar la cuarentena, mientras se encuentren asintomáticos, si bien esta decisión depende de la edad, la profesión, las variantes circulantes, el grado de contacto y el tiempo pasado desde la vacunación. En países con una alta proporción de la población vacunada se sugiere ya la posibilidad de que las personas plenamente vacunadas prescindan del uso de las mascarillas y el distanciamiento social en la mayoría de las circunstancias.

Se desaconseja la utilización de pruebas diagnósticas de manera sistemática para evaluar la respuesta inmune o el grado de protección frente a la reinfección tras la infección natural o la vacunación, dado que en este momento se ignoran sus consecuencias prácticas. La información existente hasta este momento, impide hacer cualquier precisión frente a una posible necesidad de revacunación futura.

Este Comité considera que cuando se alcance una vacunación masiva de los trabajadores sanitarios, y de la población general, podrían evitarse las pruebas de cribado de SARS-CoV-2 al menos en la actividad asistencial ambulatoria y ante procesos exploratorios que no requieren hospitalización.

Palabras clave: COVID-19, variantes virales, SARS-CoV2, escape vacunal, COVID-19 de brecha, uso de mascarillas, despistaje de COVID, vacunas, seguimiento de inmunizados

INTRODUCTION

The worldwide massive vaccination against SARS-CoV-2 infection is a milestone of historical dimension that is being made possible by the development of efficient vaccines in record time. The process, carried out in an order that prioritizes older people or those at high risk, is raising, however, some questions arising from the coexistence of two populations in our society [1-6]. On the one hand, that of vaccinated patients with a low degree of risk of contracting the disease immediately and, on the other hand, that of the population awaiting vaccination and in whom the known risks of contracting COVID-19 persist.

At the present time, it is a matter of scientific discussion, but also of political discussion, whether different attitudes should be taken with both populations, both in their medical follow-up and in the use of certain freedom of movements and social behavior. Vaccinated people do not have the same risks of contracting the disease as unvaccinated people and it is doubtful whether they require the same health monitoring and control measures.

For those reasons, the Scientific Committee of the Illustrious College of Physicians of Madrid (ICOMEM), has set out to answer some questions raised by its members using scientific evidence, where it exists, but also the experience and opinion of its partners.

HOW LONG DOES PROTECTION LAST AGAINST A NEW OR RECURRENT EPISODE OF COVID-19 IN VACCINATED PATIENTS, INFECTED PATIENTS, OR BOTH?

The duration of protection in immunized patients is a key question that has substantial implications. Laboratory studies show great heterogeneity in the magnitude of the immune response to SARS-CoV-2, with no individual factors described that can explain them well [7-9]. About 95% of patients, or vaccinated persons, produce antibodies as early as 2 weeks after the onset of infection or after vaccination [10,11].

In vitro studies show that neutralizing activity is maintained at least 6 months after infection [7] although its magnitude may be decreasing [12]. The decline in antibody titers among those who have been infected depends mainly on the intensity of the initial clinical presentation, being lower in cases where the infection has been milder [13].

In any case, memory B-cell-mediated immunity specific for spicule, RBD and nucleocapsid proteins persists after infection and will lead to a more robust antibody-mediated response in the event of a new contact with SARS-CoV-2 [7,12]. Memory B cells increase progressively after infection, stabilizing by the 4th or 5th month [14] and have been observed to persist for at least 6 months after infection [7,12]. Occasionally, the cells had not only increased in number but had undergone affinity maturation and expressed neutralizing antibodies of higher potency [12]. The T-cell response, responsible for pathogen recognition and elimination, appears 8-14 days after infection and CD8+ and CD4+ levels specific for protein S are maintained at 50% and 89%, respectively, at 6 months [7,15, 16]. Other studies demonstrate the persistence of this response nine months after infection [17] and one year after vaccination [18]. It is not well known whether the different vaccines differ in effectiveness and duration of the immune response and whether this is different from that produced by natural disease [19], although it would be expected that the behavior would be similar, at least in relation to the spike protein, to that produced as a consequence of naturally generated immunity.

WHAT IS THE SITUATION ONE YEAR LATER FOR PATIENTS WITH COVID-19 DIAGNOSED IN THE FIRST WAVE?

During the first months of the pandemic, the exceptionality of reinfections was assumed [20], but large series are now available analyzing the incidence and characteristics of reinfections. In a Danish study [21], PCR was performed on 525,239 subjects during the first wave, of whom 11,068 were positive. The population was subsequently evaluated 6 to 9 months later, and a reinfection rate of 0.65% was found among previously PCR-positive subjects, whereas in previously uninfected subjects the rate was 3.27%, with the infection estimated to provide 80% protection against reinfection. In a population-based study conducted in the United States,

3,257,478 persons were included, including 378,606 with positive serology and 2,876,773 with negative serology. After 90 days, infection rates were much lower in the serology-positive population than in those initially serology-negative, with a ratio of 0.10 (CI 0.05-0.19). Only 0.3% of seropositive patients had a positive PCR at follow-up, compared to 3% of the initially seronegative population [22]. Finally, in a study of 12,541 healthcare workers [23], 11,276 of whom had no evidence of previous infection and 1,177 were positive, there were only 3 cases of reinfection in those previously infected compared to 218 in the group of workers who were basically seronegative for SARS-CoV-2. Nine months after the start of the study, the estimated incidence of reinfection for 10,000 days of exposure was 0.07 in the basally positive patients, compared to 1.08 in the initially seronegative patients, giving a relative risk of 0.11 (0.03-0.44).

Using genomic typing, reinfection was very rare in a cohort studied in Marseille in which 6,771 cases diagnosed with COVID-19 by PCR during the first wave were followed up [24]. In 9 months of follow-up, reinfection was demonstrated in 46 of them (0.51%) which were due to the local dominant variant.

In relation to possible risk factors, it seems that cases of reinfection are more frequent when the previous infection has been mild, when exposure is important and in the presence of immunosuppression, but in reality the cases are so few that it is difficult to draw firm conclusions. The same is true with regard to clinical features and severity.

The problem of reinfections must be followed over time, since it is to be expected that these will increase as a consequence of the decline of the immune response and also because of the impact that new variants may have, although this also needs to be confirmed.

WHAT HAS BEEN THE IMPACT OF VACCINATION IN COUNTRIES THAT HAVE EXCEEDED 70% VACCINATION COVERAGE?

There is still little data on the impact of vaccination in countries with high vaccination rates. The most recent dynamic data highlight that the countries with the highest percentage of population vaccinated with a single dose are Malta (71.1%), Israel (63.0%), England (57.8%), Canada (55.5%) or Chile (54%) and with complete vaccination are Israel (59.3%), Malta (45.3%), Chile (41.3%), the United States (38.8%) and the United Arab Emirates 38.8%[25]. Some of these countries have published data on the impact of vaccination on the rate of SARS-CoV-2 infection as well as other disease outcomes.

A simulated study using demographic data from the United States evaluates the impact of a COVID-19 vaccination campaign with two doses of vaccine. Vaccination would reduce the attack rate from 9% to 4.6% (95% CrI: 4.3% - 5.0%) over 300 days. The highest relative reduction would be among those over 65 years of age. In addition, vaccination would reduce the rate of hospitalization, ICU admission, and deaths by 63.5%, 65.6%, and 69.3%, respectively, over the same period. The authors conclude that vaccination can have a substantial impact on mitigating COVID-19 outbreaks, even with limited protection against infection [26].

The SIREN study [27] is a prospective cohort study analyzing the impact of vaccination against SARS-CoV-2 in healthcare professionals in public hospitals in the United Kingdom. After achieving a vaccination coverage of 89% (94% immunized with the BNT162b2b2 mRNA vaccine), the authors found an infection incidence rate of 8/10,000 person-days 21 days after the first dose and 4/10,000 person-days 7 days after the second dose, compared to 14/10,000 person-days in the unvaccinated group. With this, vaccine effectiveness against all infections (symptomatic and asymptomatic) is estimated at 70% (95% CI 55-85) at 21 days after the first dose and up to 85% (95% CI 74-96) at 7 days after the second dose [27].

On December 20, 2020, Israel launched its national vaccination campaign, against COVID-19, with BNT162b2 vaccine [28]. It was implemented in the entire population selected by the Israeli Ministry of Health and, within two months, 48% of the population over 16 years of age had received full vaccination, 68.7% had at least one dose and 8% were unvaccinated patients. The vaccination campaign was initiated prioritizing the over-60s and the at-risk population. Two doses of BNT162b2 vaccine were highly effective in all age groups in preventing symptomatic and asymptomatic SARS-CoV-2 infections, COVID-19-related hospitalizations, severe illness and death, including those caused by SARS-CoV-2 variant B.1.1.7.

ARE THERE DIFFERENCES IN THE DURATION OF PROTECTION BETWEEN VACCINES?

To date, there are no studies available that directly compare the protection and duration of protection against COVID-19 between the different vaccines. In the clinical trials published to date, the comparator has always been placebo, although in the future trials this may no longer be the case.

The mRNA-1273 8 vaccine (Moderna, Inc) is the only vaccine that has published data on the duration of immunity. In a study of 33 healthy adults participating in a phase I study, the activity of protein S receptor binding domain (RDB) binding antibodies and neutralizing antibodies remained elevated 180 days after the second application of 100 µg of vaccine (day 209) [29].

There are no published data on the duration of BNT162b2 vaccine (Pfizer/BioNTech). However, the company has issued a press release announcing the interim results of the phase 3 extension of the clinical trial. Among the 927 confirmed symptomatic cases of COVID-19 observed in the Phase 3 study, the vaccine was 91.3% effective against COVID-19 and 100% effective against severe infection as defined by the CDC and 95.3% as defined by the FDA. Measurements were performed between seven days and six months after the second dose [30]. These results are pending scientific peer review and possible future publication.

Ad26.COV2. S vaccine (Janssen Vaccines & Prevention B.V./ Johnson & Johnson) offers an efficacy from 28 days after administration of approximately 66% in preventing moderate

to severe/critical forms of COVID-19, and 85% in preventing severe and critical forms [31]. The study showed that efficacy continued to increase for 8 weeks after administration, especially for severe and critical COVID-19. No decrease in efficacy was observed among 3,000 vaccinees followed for 11 weeks or among 1,000 vaccinees followed for 15 weeks [31].

There are no studies evaluating the duration of protection of the ChAdOx1 nCoV-19 vaccine (Oxford Vaccine Group/AstraZeneca). The vaccine shows an overall efficacy to protect against symptomatic disease of 63.1% (51.8-71.7) and 100% efficacy to prevent severe cases, starting 2 weeks after the 2nd dose [32].

WHAT IS THE RISK OF TRANSMISSION OF SARS-CoV-2 TO NAÏVE PERSONS FROM VACCINATED PATIENTS WHO ACQUIRE ASYMPTOMATIC OR OLIGOSYMPTOMATIC INFECTION?

There is some indirect evidence that in infections in vaccinated persons there may be a reduced risk of SARS-CoV-2 virus transmission. First, the viral load of the relatively few vaccinated persons who become infected is generally lower than that of unvaccinated infectees [33]; this suggests lower infectivity, either because any transmission requires sufficient inoculum or because presumably the duration of the transmission period is shorter. Second, vaccination has been shown to reduce the risk of infection, both symptomatic and asymptomatic [34]. In principle, the uninfected should not be able to infect.

In Scotland, COVID-19 cases and hospitalizations in (unvaccinated) household members of vaccinated healthcare workers have been identified from December 8, 2020, to March 3, 2021. Within 14 days of the first dose of the healthcare worker vaccine, a 30% reduction in COVID-19 cases (27% in hospitalizations) was observed in household contacts, consistent with an effect of vaccination on transmission [35].

In another study, in England, the proportion of household contacts who had a positive PCR between 2 and 14 days after the index cases had been vaccinated was analyzed and compared with infections in households in which the index case was not vaccinated. Adults infected with SARS-CoV-2 three weeks after receiving a dose of Pfizer-BioNTech or Oxford-AstraZeneca vaccine were 38-49% less likely to transmit the virus to their household contacts than unvaccinated index cases. The results were similar regardless of the age of the cases or contacts [36,37].

It is noteworthy that the reduction in transmission in the few infected subjects after vaccination is probably greater than that observed in these two studies, as these were done after a first dose of vaccine, and the reduction in transmission is expected to be even greater after the second dose. On the other hand, the evidence has been obtained in the scenario of highest possible transmission, since both the index cases and their contacts shared a home, where people do not usually wear masks and the physical distance is very small.

This type of evidence (significant reduction in the risk of infection and transmission by vaccinees) has contributed in the United States of America to the lifting of the obligation for vaccinees to wear masks, especially outdoors, and to maintain physical distance, both outdoors and in most enclosed spaces [38,39].

IS CONFINEMENT OF VACCINATED OR PREVIOUSLY INFECTED PATIENTS JUSTIFIED AFTER CONTACT WITH A PATIENT WITH ACUTE SARS-CoV-2 INFECTION?

The risk of infection in a fully vaccinated person or a person who has had COVID-19 and who has contact with a person with active SARS-CoV-2 infection is low. Depending on the vaccine used and the characteristics of the population, it ranges from 5% to 28% (the reinfection rate may be even lower). This has allowed some agencies to relax the measures to be taken after documented contact [39, 40]. In the opinion of this Committee and with the information currently available, it is considered that factors that may modify the risk of infection and the severity for the individual and his or her potential contacts whom he or she might infect should be considered in making the decision to isolate and quarantine in this situation. Factors to be considered in establishing the indication for isolation and quarantine include:

- Place of residence or work: for residents or workers in healthcare or social-healthcare facilities, isolation and quarantine should still be considered if there has been well-documented close contact with a person with active SARS-CoV-2 infection.

- Immunosuppression status: immunosuppressed persons may have had a worse response to the vaccine and are at increased risk of infection.

- Age: the risk of not producing an adequate immune response is higher at older ages.

- Circulating variants: these may be variants against which protective immunity is potentially not induced by the vaccines used.

- Vaccine type: vaccines offer different degrees of protection and may protect differently against some circulating variants.

- Degree of contact: the risk of infection varies with the duration and intimacy of the contact (cohabitant in the same household, occasional outdoor contact,...).

- Time since vaccination: the duration of protection is unknown. The longer the time since vaccination, the higher the risk of infection due to the disappearance of immunity.

Thus, vaccinated persons who have had close contact with a patient with active COVID do not have to undergo quarantine or isolation, except in the circumstances previously mentioned or if they present symptoms compatible with SARS-CoV-2 infection. In the latter case, isolation and diagnostic testing for COVID-19 should be performed.

IS THERE A REASON TO PROHIBIT SOCIAL AND WORK MEETINGS BETWEEN VACCINATED OR PREVIOUSLY INFECTED PEOPLE?

In the United States of America, 101 million people have

been vaccinated as of April 30, 2021, and CDC is aware of 10,262 SARS-CoV-2 gap infections in fully vaccinated persons (0.01%). Twenty-seven percent of those gap infections were asymptomatic and only 1.5% of the total infected died [41].

On this basis, the CDC has just released its recommendations for vaccinated patients [39] which include the recommendation that these individuals resume their activities without wearing masks or physically distancing themselves, except when required by applicable regulations. They also recommend resuming domestic travel and refraining from pre- or post-travel testing or self-quarantine after travel. We believe that in Spain, once similar conditions to those in the United States in terms of vaccination and transmission have been achieved, these recommendations can be taken on board, although the sensible application of these measures requires the responsibility of all [42].

For the time being, fully vaccinated individuals should continue to be tested for COVID-19 if they experience compatible symptoms and follow existing travel health requirements and recommendations.

Mathematical simulations suggest that vaccination of at least 75% of the population is necessary for the vaccine to be the only pandemic control measure (making all others unnecessary) [43,44].

WHAT IS THE APPROPRIATE POLICY FOR FOLLOW-UP WITH LABORATORY TESTING OF VACCINATED OR PREVIOUSLY INFECTED PATIENTS?

Although some studies show a high correlation between IgG production and neutralizing activity [45] against the virus, current serological diagnostic tests against SARS-CoV-2 have limitations in estimating such activity [10,11,46,47]. In addition, the level of neutralizing antibodies that protect against COVID-19 infection or reinfection is unknown [11,47]. On the other hand, the presence of antibodies can decline significantly over time without necessarily leading to loss of neutralizing activity [47,48] and several studies have shown that B and T cell memory, remain for a period of at least 8 to 10 months after natural or vaccinal infection [7,11, 29,48,49].

In summary, the duration of protective immunity and immune memory after COVID-19 infection and the ability of diagnostic tests to predict it are unknown [10]. Therefore, the use of such tests to assess the immune response after vaccination or the degree of protection against reinfection after the first infection is generally discouraged [50,51]. At present, a low antibody titer is not a recommendation to administer additional doses of the same or other vaccines or to decide between one or two doses in vaccines where two doses are recommended [51].

WHAT IS EXPECTED FROM CELLULAR IMMUNITY TESTING IN PATIENTS IMMUNIZED AGAINST SARS-CoV-2?

Cell-mediated immunity appears to be an important part of the immune response to SARS-CoV-2 whether naturally occurring or vaccine-induced. In natural infection, effective virus clearance appears to require collaboration between humoral and cellular responses [52]. CD8+ T-cell depletion in convalescent macaques partially abrogates the protective efficacy of natural immunity against re-exposure to SARS-CoV-2, suggesting a role for cellular immunity in the context of declining or subprotective antibody titers and indicating that cellular immune responses may contribute to protection if antibody responses are suboptimal [53].

Cell-mediated immunity by itself does not prevent infection, but it is important in clearing it once it has begun. They can make the difference between a mild infection and a severe one requiring hospital treatment. If the cellular response is able to eliminate infected cells before the virus spreads through the body, it will influence the course of the disease. It could also reduce transmission by restricting the amount of circulating virus, which would mean that it would spread fewer viral particles in the community.

Multiple studies suggest that circulating antibodies to coronaviruses may be short-lived or of low magnitude and potency [54, 55]. Therefore, rapid expansion of vaccine-induced memory lymphocytes may be needed to stimulate immunity and reduce disease and COVID-19 transmission [56,57].

For these reasons, one of the main goals of vaccines against SARS-CoV-2 should be to induce memory T cells both in the circulation and in tissues. Initial studies with the different vaccines already marketed demonstrated the induction of a sufficient cellular response. It is now important to monitor the stability of memory T cells over months and years in animal models and in humans. Work in SARS suggests that memory T cells against SARS-CoV-2 are long-lived, but more research and more time are required for full evaluation of the duration of immunity to SARS-CoV-2 [58]. Unfortunately, at this time, we do not yet have simple tests for routine clinical application to measure the cell-mediated immune response in patients immunized against COVID [59].

WHAT WOULD BE THE REASONS AND TIMING OF NEW BOOSTER DOSES?

We have just commented that the time of protection due to both natural immunity and vaccination or the association of the two is not precisely known. Nor do we have any routine test that would help us to mark the beginning of a state of unprotection and risk of reinfection. Taking as an example a long-term epidemiological study (35 years) on immunity to other seasonal coronaviruses and evaluating the frequency of reinfection by sampling every 3 to 6 months, it was concluded that protective immunity is short-lived and natural reinfections occurred more frequently after 12 months [60]. We do not know if this case of one type of coronavirus represents all others and in particular SARS-CoV-2.

The aspects discussed above would open up the possibility that the administration of booster doses of existing vaccines or the administration of new vaccines adapted to the new variants that might appear might be necessary, but at this time both possibilities, in our opinion, remain speculative. Very re-

cent data would allow us to be even more optimistic about the persistence of the immunity provided by natural infection or current vaccines [61].

IN VACCINATED PATIENTS OR PATIENTS WITH PAST INFECTION WHO ARE GOING TO UNDERGO SURGERY OR INVASIVE TESTS, ARE COVID SCREENING TESTS NECESSARY PRIOR TO SURGERY OR INVASIVE TESTS?

The hospital environment has nothing to do with other scenarios of everyday life, and therefore it is necessary to adapt protection measures to the environment in which we move. In general, hospitals must remain safe places, since patients are a more vulnerable population in themselves. It is essential to keep the "clean" areas separate from the "contaminated" areas (COVID-19 inpatient wards) in order to be able to provide good and safe care. To achieve this, hospitals have implemented a series of measures that have made it possible to reduce the risk of nosocomial infection to a minimum. These measures include screening with PCR tests for patients who are going to undergo surgery, invasive tests that generate aerosols (endoscopy, spirometry, etc.) or require hospital admission. In addition to giving them specific recommendations on limiting contacts, use of masks, etc.

The appearance of vaccines that reduce the risk of severe disease and hospitalization [33,62,63] and the publications that point out that vaccinated persons can contract the infection but usually have a very low viral load [33], is countered by the fact that this risk is not zero.

We believe that at this time, in the hospital setting, it is necessary to continue to maintain the recommendations and screening with PCR (currently the most specific and sensitive test) for the group of patients who are going to undergo surgery, hospitalization, etc., in order to avoid possible in-hospital outbreaks. It is important to take into account, when maintaining this measure, the percentage of the population vaccinated.

Another different scenario is hospital outpatient care of vaccinated patients. As previously mentioned, before the patient undergoes any diagnostic-therapeutic test that generates aerosols, minor surgery or major outpatient surgery, he/she is screened with PCR. In this case the risk of transmission, professional-patient or vice versa, is even lower, since both groups are usually vaccinated. Moreover, these procedures are performed in areas where there is no contact with hospitalized patients. It is in this context that this committee is of the opinion that PCR could be omitted prior to the performance of these outpatient procedures, maintaining only the standard prevention measures.

WHAT SHOULD BE THE ATTITUDE TOWARDS VACCINATED PATIENTS IN WHOSE EVOLUTION THE ABSENCE OF ANTIBODIES IS DETECTED?

As previously discussed, the use of antibody titer measurement tests to assess the immune response after vaccination or the degree of protection against reinfection after the first infection is discouraged [50,51]. Protection against COVID-19 by vaccination is not 100%, which means that with current vaccines there is a variable percentage of COVID-19 gap. This situation is common in almost all vaccine-preventable diseases. In these patients, it does not seem plausible or indicated to perform a new vaccination with a different model (RNA-attenuated virus and vice versa), or to administer booster doses of vaccine, as mentioned above.

True protection in these situations will be provided by the environment when the degree of vaccination reaches at least 75% of the population. Therefore, in these patients in whom the risk of gap COVID-19 is higher [64], it would be advisable to maximize the usual preventive measures.

CONCLUSIONS

1.- As a consequence of the activation of the immune response in patients vaccinated or infected with SARS-CoV-2, the occurrence of reinfections in the observation period available to date (6 to 15 months) is very low. This is demonstrated by data from countries with already very high rates of vaccinated population.

2.- Gap infections in patients with previous infection, vaccinated, or both, are generally asymptomatic or paucisymptomatic and potentially have a lower capacity of transmission to non-immunized persons, as a consequence of presenting a lower inoculum.

3.- There are no comparative studies between vaccines that can demonstrate differences in the duration of protection between them.

4.- The use of serological tests indiscriminately for the follow-up of patients after natural infection or vaccination is discouraged, since their clinical significance and practical consequences are not known at this time.

5.- Data from countries with a high proportion of the population vaccinated suggest the possibility that fully vaccinated persons can be dispensed with the use of masks and social distancing in most circumstances. They can also avoid quarantine after contact with infected patients with exceptions, determined by type of work, advanced age or immunosuppression, among others.

6.- The need for revaccination with the same or new vaccines is, at this time, merely speculative, since the existing information prevents any precision on this subject.

7.- PCR screening of patients to be hospitalized should be maintained for the time being in order to avoid nosocomial outbreaks, until community transmission rates in our environment fall further. On the other hand, this Committee considers that screening tests could be avoided in outpatient activity where the contact of the vaccinated patient is restricted to health personnel, who are also vaccinated.

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CONFLICTS OF INTEREST

The authors declare no conflicts of interest

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