Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

COMMENTARY

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Lack of Convincing Evidence That the Widely Used COVID-19 Vaccines Will Produce Herd Immunity

Two mRNA vaccines are in wide usage in the United States and elsewhere.[1-5] In the initial clinical trials these 2 vaccines were found to have a high level of efficacy for prevention of symptomatic infection caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), that is, COVID-19 infection. The efficacy of each of the 2-dose mRNA vaccines for prevention of symptomatic infection was more than 90% at approximately 2 months after the second vaccine dose.[2,3,6] Although also efficacious in preventing asymptomatic infections, the level of efficacy was lower at 63.0% (95% confidence interval: 56.6%-68.5%).[5] Asymptomatic infections are important because they can lead to transmission to others.[7] However, the efficacy declined fairly rapidly over the next few months; consequently a third dose (booster dose) is now widely used to restore a high degree of vaccine efficacy in the United States.[8] And even a fourth dose is now being used in Israel. A third vaccine not based on mRNA is also available in the United States.[8]

Coincident with the arrival of the omicron variant of SARS-CoV-2 late in 2021, the number of COVID-19 cases per day reached the highest values in the United States seen thus far. The remarkable spike in the number of identified cases seems to be occurring primarily among persons who have been vaccinated, which is likely not surprising because this group comprises the majority of the adult population.

One illustrative example of the remarkable potential for the spread of SARS-CoV-2 despite vaccination is as follows. In mid-December 2021 a group of 30 graduate students, ages 29-45 years, attended their first in-person class in more than 4 weeks. During the 8-hour class the students presented their research projects. Vaccination was required of all students prior to attendance, and all had to have tested negative for SARS-CoV-2 on a saliva sample within 24 hours before arriving at the classroom. Five teaching staff members were also present for the duration of the 8-hour class, as well as approximately 5 student mentors who attended for up to 5 hours of the class, and approximately 10 student spouses who each attended for about 1 hour. Vaccination was required of all the nonstudent attendees, but it is unknown whether they were also required to have a negative COVID-19 test prior to attending. All attendees wore a face mask during the entire time spent in the classroom except while eating; they also did not wear masks while attending a party at another location that took place after the class was finished. This party included additional student family members.

Seven of the 30 students developed mild symptoms consistent with COVID-19 within 48-72 hours of attending the class, and 6 tested positive for COVID-19 (ie, 20% of the students developed COVID-19). Three other students developed symptoms between days 5 and 10 following the class and also tested positive for COVID-19. The SARS-CoV-2 variant causing these infections was not determined.

In addition, among the 7 friends and coworkers of 1 of the coauthors (GPW) who were symptomatic and diagnosed with COVID-19 during December 2021, all had been fully vaccinated and all had received the booster dose. Five (71.4%) had received the booster dose at least 14 days prior to onset of symptoms.

Information that would explain what is currently being widely observed is becoming available. A relevant study of COVID-19 vaccine effectiveness over time was conducted in the United States Veterans Health Administration.[9] From February to October 2021, vaccine efficacy for the 2 mRNA vaccines dropped. Specifically, in March of 2021 the mRNA vaccine efficacy rates for prevention of symptomatic COVID-19 infection was 86.9%-89.2%; by September 2021, however, the efficacy rates had declined to 43.3% to 58.0%. During the delta variant surge, however, vaccination continued to demonstrate at least moderate

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efficacy in providing protection from death. From July to October 2021, vaccine effectiveness for the 2 mRNA vaccines against death for those at least 65 years of age was 70.1%-75.5%.

Nevertheless, the falling efficacy over such relatively short time periods, along with the emergence of the delta variant,[9-11] has justified increasing attention to maintaining non-pharmaceutical approaches (such as wearing masks and social distancing) to reduce new infections. However, data emerging on the omicron variant are even more concerning. The UK Health Security Agency has suggested that protection against symptomatic disease at 25 weeks after 2 vaccine doses might be less than 10% for the omicron variant, compared with 40% for the delta variant.[12] This reinforces the concept of booster dosing for recipients of an mRNA vaccine,[8,9] although the exact efficacy of booster doses to prevent omicron infection has not as yet been established. Future studies might also attempt to correlate the level of the immune response to the level of protection observed clinically, allowing a more precise determination of who in the future might require additional vaccine doses and when.

SARS-CoV-2 strain differences that impact contagiousness have a substantive impact on the proportion of a population group that need to be fully protected to achieve herd immunity. At the beginning of the pandemic the reproductive number was estimated to be 2.5,[12] implying that herd immunity could be achieved if only approximately 60% of the population had immunity (natural or vaccine-derived). Estimates for the reproductive number for the more contagious delta variant are close to 7,[12] implying that approximately 85% of the population would need to be immune to infection to achieve herd immunity, rising to approximately 90% for the omicron variant, whose estimated reproductive number could be as high as 10.[12] Ninety percent of the population achieving long-lasting immunity seems rather unrealistic with the vaccines currently available, raising concerns that herd immunity is not a realistic answer to ending this pandemic. However, new approaches to vaccine development are in progress, which might impact this in a more favorable manner.[13] In addition, rapid spread of a minimally virulent but highly contagious strain of SARS-CoV-2 might per se also promote widespread immunity,[14] including for those who prefer not to be vaccinated. Natural infection with SARS-CoV-2 has been shown to be highly protective against a recurrence of symptomatic infection, with an efficacy rate of 84.5% in 1 study (95% confidence interval: 77.9%-89.1%).[15] Studies of patients during the SARS pandemic in 2003 found that an antibody response from this infection persisted for 2 years.[15] Infections with the seasonal strains of coronavirus, however, do not lead to the development of long-term protection.[15] Whether the recent and rapid spread of omicron might promote widespread immunity against a future infection caused by a different strain of SARS-CoV-2 is an open question, but unfortunately it appears that the omicron variant does not invariably cause a benign infection.[16]

In conclusion, the efficacy of the currently available mRNA vaccines for prevention of symptomatic COVID-19 infections falls over relatively short periods of time. Efficacy is also highly dependent on the particular variant of SARS-CoV-2 that a person is exposed to. Although these vaccines have been successful in reducing hospitalization and death, the likelihood of developing herd immunity using the currently available vaccines appears to be low.

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