PERSPECTIVE

National Science Open
1: 20220007, 2022
https://doi.org/10.1360/nso/20220007

Life Sciences and Medicine

Special Topic: COVID-19: Virus, Immunity and Vaccines

One year of COVID-19 vaccination

Meng-Li Cheng, Hui Zhao & Cheng-Feng Qin*

State Key Laboratory of Pathogen and Biosecurity, Beijing Institute of Microbiology and Epidemiology, Academy of Military Medical Sciences, Beijing 100071, China

*Corresponding author (email: qincf@bmi.ac.cn)

Received: 2 November 2021; Revised: 6 January 2022; Accepted: 18 January 2022; Published online: 24 March 2022

Abstract: The year 2021 saw the development and deployment of COVID-19 vaccines at an unprecedented pace, which is a remarkable success in science and technology. COVID-19 vaccines based on different technology platforms have been given to billions of humans globally to minimize the infection and transmission of SARS-CoV-2, and most importantly, to end the COVID-19 pandemic. Here, we provide a snapshot of the current status and future challenge of COVID-19 vaccination after one year.

Keywords: SARS-CoV-2, COVID-19, vaccine, VOCs, immune response

Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is still spreading worldwide, with more than 275 million confirmed cases and 5.3 million mortalities in the 2 years since it was first identified in December 2019 [1–3]. It was evident early that only effective vaccines can control the global pandemic, which resulted in an unprecedented pace of vaccine development. Currently, there are 137 candidate COVID-19 vaccines in clinical trials, of which 39 are undergoing phase 3 or 4 trials, and an additional 194 vaccine candidates are in preclinical studies [4]. On 31 December 2020, the first COVID-19 vaccine was approved for emergency use authorization (EUA) by the US FDA. After one year of COVID-19 vaccination, it is time to rethink the factors associated with the virus and vaccines.

COVID-19 vaccines are designed to elicit immune responses, ideally by stimulating the production of binding antibodies and neutralizing antibodies against the SARS-CoV-2 spike protein, as well as stimulating virus-specific T cell responses. Currently, 19 vaccines were approved for EUA in China, the US, the EU, India, etc. These vaccines include mRNA vaccines, whole-virus inactivated vaccines, adenoviral-vectored vaccines and subunit protein vaccines [4]. The vaccine efficacies ranged from 50% to 95% according to phase III clinical trials [4]. As of 21 December 2021, a total of 8.7 billion vaccine doses have been administered globally, 56.8% of the world population has received at least one dose of a COVID-19 vaccine, and 34.8 million doses are now administered each day [5]. On 23 August 2021, the FDA granted full approval to the mRNA-based COVID-19 vaccine developed by BioNTech and Pfizer. Since then, the causative cases and deaths of COVID-19 have been decreasing [3,4] due to the mass vaccination campaigns and other uncertain factors.

COVID-19 vaccines that are approved for emergency use have demonstrated an acceptable safety profile with local or systemic minor acute reactions. Certain adverse events, due to rarity or pathogenesis, might be detected only during long-term surveillance. Owing to the accelerated development process, interim data from ongoing clinical and preclinical vaccine studies are being published almost in real time, which calls for real-time safety surveillance of COVID-19 vaccines, as well as long-term monitoring. As the vaccinated population increases and as longer safety studies are carried out, some rare cases of potential serious adverse effects associated with the vaccines are seen once millions of individuals have been vaccinated, and these serious adverse reactions include anaphylaxis, myocarditis, and thrombotic thrombocytopenia outcomes associated with mRNA or vector vaccines [6–8]. Most cases of anaphylaxis were in women (63 of 66) [7], and myocarditis was possibly associated with younger individuals receiving mRNA vaccines, both of which had no deaths reported. In March 2021, the European Medicines agency concluded that in an extremely small number of vaccinated individuals, there is a causal link between AZD1222 administration, blood clotting and low platelet counts (thrombocytopenia), which led to 30 deaths in vaccinated individuals, and these adverse reactions were also observed in the USA [9–12], with patients developing the characteristics of heparin-induced thrombocytopenia and detectable levels of antibodies to the heparin–platelet factor 4 complex [13]. A recent study found that the combination of AZD1222 and BNT162b2 vaccines increased the reactogenicity of heterologous prime–boost regimens compared with homologous vaccination [14]. Overall, the benefits of avoiding COVID-19 by vaccination far outweigh the theoretical risk of vaccines, and the safety of COVID-19 vaccines needs to be monitored over time.

Although the exact initial source of SARS-CoV-2 remains elusive, SARS-CoV-2 continues to evolve while it circulates globally. In particular, the emergence of the most paramount variants of concern (VOCs), including the alpha (B.1.1.7), beta (B.1.351), gamma (P.1) and delta (B.1.617.2) variants [15], has aroused global concerns. The predominant mutations of these VOCs were in the S protein when compared with the reference strain, and these mutations could enhance the interactions with the host receptor ACE2, increase viral transmissibility or reduce the potency of neutralizing antibodies, thereby compromising vaccine efficacy. There are increasing breakthrough infections with VOCs in vaccinated individuals. Limited data has shown that the protection efficacy of mRNA vaccines, adenoviral-vectored vaccines or subunit protein vaccines was 70–90% and 10–75% for alpha and beta VOCs, respectively, of which adenoviral-vectored vaccines or whole-virus inactivated vaccines was 51–68% for gamma VOCs, and the protection effectiveness was 60–92% for delta VOCs [6,8]. Increased transmission and vaccine escape may be the main selective pressure to accelerate more VOCs, especially when total global vaccine coverage is imbalanced. Interestingly, the convergent evolution of SARS-CoV-2 emerged during human transmission and animal adaption [16], highlighting the uncertainty of next variant to emerge.

What should we do to counteract the known and forthcoming VOCs? One strategy is to boost immunity with one more dose of the first-generation vaccines targeted to the initial reference strain. Whether the additional booster dose should be the same vaccine as the initial course or should be with a heterologous platform represents the wisdom of risk-benefit assessment. Novel vaccines based on the protective antigens of VOCs are also being designed and evaluated by different vaccine companies.

The development and deployment of COVID-19 vaccines of various platforms represent a remarkable landmark, but there are still many questions to be addressed. First, the mechanisms of vaccination-medicated protection and breakthrough infection remains to be fully understood. The difference between administration

of one *versus* two doses and even when another homologous or heterologous booster dose is given, and a complete understanding will enable decisions on the vaccination gap. A recent study found that the antibody response is greater in individuals aged 80 years or older when the vaccination gap increases from 3 to 12 weeks [17], indicating that extended interval vaccination in senior individuals may be a rational strategy. Second, clinical trials of COVID-19 vaccines have focused on younger and healthy adults, but the outcomes of patients with immune-mediated inflammatory disease, B cell-depleting therapies, or concurrent biologic use, showed COVID-19 vaccine safety profiles that were comparable to those of healthy controls [18–21], although there was a reduction in antibody and neutralization titers. However, it is more important to show that these factors are not contraindications to vaccination [22]. Clinical trials of COVID-19 vaccines in different age groups and populations are important to understand the extent and duration of protection against infection or disease, which is also beneficial to predict protection in specific populations, such as children, pregnant women and immunocompromised individuals. Third, SARS-CoV-2 can spread from cell to cell without exposure to the extracellular environment [23], so the role of neutralization antibodies was limited in reducing the viral spread between cells. T cells are also important mediators in the host response to SARS-CoV-2 infection, and memory T and B cells have been present for more than one year in recovered patients [24,25]. Furthermore, there was no significant difference in the memory T cell responses between the original strain and VOCs [26,27]. Additionally, the mechanisms of protection induced by COVID-19 vaccines are still not completely clear, so the measurable correlate of protection that reliably predicts the protection against COVID-19 after vaccination or natural infection has not yet been defined. More openly available original data are urgently required to better understand the mechanism of protection and to compare the efficacy and effectiveness of the different vaccine platforms. Last but not least, currently, only 7.6% of people in low-income countries have received at least one dose [5]. Thus, more vaccines need to be distributed to low-income countries. What is more important is to improve these countries' capacity for pandemic response, including the transfer of technology and manufacturing capability.

Funding

Research in Dr Cheng-Feng Qin's laboratory was supported by the National Key Research and Development Project of China (2021YFC0865800, 2020YFC0842200, 2020YFA0707801, 2021YFC0863300, and 2021YFC2302400) and the National Natural Science Foundation of China (NSFC)(82041044 and 82151222). C.F.Q. was supported by the National Science Fund for Distinguished Young Scholars (81925025), the Innovative Research Group (81621005) from the NSFC, and the Innovation Fund for Medical Sciences (2019-I2M-5-049) from the Chinese Academy of Medical Sciences.

Author contributions

M.L.C., C.F.Q. and H.Z. contributed to manuscript writing. All authors reviewed and approved the final version of the manuscript.

Conflict of interest

The authors declare that there is no conflict of interest.

References

1 Wang C, Horby PW, Hayden FG, *et al.* A novel coronavirus outbreak of global health concern. *Lancet* 2020; **395**: 470–

473.

2 Zhu N, Zhang D, Wang W, *et al.* A novel coronavirus from patients with pneumonia in China, 2019. *N Engl J Med* 2020; **382**: 727–733.

3 Johns Hopkins University. Coronavirus Resource Center. https://www.arcgis.com/apps/dashboards/bda7594740fd40299423467b48e9ecf6. 2021.

4 World Health Organisation. COVID-19 vaccine tracker and landscape. https://www.who.int/publications/m/item/draft-landscape-of-covid-19-candidate-vaccines. 2021.

5 Ritchie H, Mathieu E, Rodés-Guirao L, *et al*. Coronavirus pandemic (COVID-19). Published online at OurWorldInData.org. https://ourworldindata.org/coronavirus. 2020.

6 Bok K, Sitar S, Graham BS, *et al.* Accelerated COVID-19 vaccine development: milestones, lessons, and prospects. *Immunity* 2021; **54**: 1636–1651.

7 Shimabukuro TT, Cole M, Su JR. Reports of anaphylaxis after receipt of mRNA COVID-19 vaccines in the US—December 14, 2020–January 18, 2021. *JAMA* 2021; **325**: 1101.

8 Tregoning JS, Flight KE, Higham SL, *et al.* Progress of the COVID-19 vaccine effort: viruses, vaccines and variants versus efficacy, effectiveness and escape. *Nat Rev Immunol* 2021; **21**: 626–636.

9 European Medicines Agency. DHPC: COVID-19 vaccine AstraZeneca: risk of thrombocytopenia and coagulation disorders. https://www.ema.europa.eu/en/medicines/dhpc/vaxzevria-previously-covid-19-vaccineastrazeneca-risk-thrombocytopenia-coagulationdisorders. 2021.

10 Food and Drug Administration. Joint CDC and FDA statement on Johnson & Johnson COVID-19 vaccine. https://www.fda.gov/news-events/press-announcements/joint-cdc-and-fda-statement-johnson-johnson-covid-19-vaccine. 2021.

11 Lee EJ, Cines DB, Gernsheimer T, *et al.* Thrombocytopenia following Pfizer and Moderna SARS-CoV-2 vaccination. *Am J Hematol* 2021; **96**: 534–537.

12 Shay DK, Gee J, Su JR, *et al*. Safety monitoring of the Janssen (Johnson & Johnson) COVID-19 vaccine—United States, March–April 2021. *MMWR Morb Mortal Wkly Rep* 2021, **70**: 680–684.

13 Scully M, Singh D, Lown R, *et al.* Pathologic antibodies to platelet factor 4 after ChAdOx1 nCoV-19 vaccination. *N Engl J Med* 2021; **384**: 2202–2211.

14 Shaw RH, Stuart A, Greenland M, *et al.* Heterologous prime-boost COVID-19 vaccination: initial reactogenicity data. *Lancet* 2021; **397**: 2043–2046.

15 World Health Organization. Tracking SARS-CoV-2 variants. https://www.who.int/en/activities/trackingSARS-CoV-2-variants/. 2021.

16 Zhou HY, Ji CY, Fan H, *et al.* Convergent evolution of SARS-CoV-2 in human and animals. *Protein Cell* 2021; **12**: 832–835.

17 Parry H, Bruton R, Stephens C, *et al.* Extended interval BNT162b2 vaccination enhances peak antibody generation. *NPJ Vaccines* 2022; **7**: 14.

18 Boekel L, Kummer LY, van Dam KPJ, *et al.* Adverse events after first COVID-19 vaccination in patients with autoimmune diseases. *Lancet Rheumatol* 2021; **3**: e542–e545.

19 Connolly CM, Ruddy JA, Boyarsky BJ, *et al.* Safety of the first dose of mRNA SARS-CoV-2 vaccines in patients with rheumatic and musculoskeletal diseases. *Ann Rheum Dis* 2021; **80**: 1100–1101.

20 Damiani G, Allocco F, Malagoli P. COVID-19 vaccination and patients with psoriasis under biologics: real-life evidence on safety and effectiveness from Italian vaccinated healthcare workers. *Clin Exp Dermatol* 2021; **46**: 1106–1108.

21 Watad A, De Marco G, Mahajna H, *et al.* Immune-mediated disease flares or new-onset disease in 27 subjects following mRNA/DNA SARS-CoV-2 vaccination. *Vaccines* 2021; **9**: 435.

22 Wack S, Patton T, Ferris LK. COVID-19 vaccine safety and efficacy in patients with immune-mediated inflammatory disease: review of available evidence. *J Am Acad Dermatol* 2021; **85**: 1274–1284.

23 Fenrich M, Mrdenovic S, Balog M, *et al.* SARS-CoV-2 dissemination through peripheral nerves explains multiple organ injury. *Front Cell Neurosci* 2020; **14**: 229.

24 Cañete PF, Vinuesa CG. COVID-19 makes B cells forget, but T cells remember. *Cell* 2020; **183**: 13–15.

25 Zhang, J, Lin, H, Ye, B, *et al*. One-year sustained cellular and humoral immunities of COVID-19 convalescents. *Clin Infect Dis* 2021; https://doi.org/10.1093/cid/ciab884.

26 Bertoletti A, Le Bert N, Qui M, *et al.* SARS-CoV-2-specific T cells in infection and vaccination. *Cell Mol Immunol* 2021; **18**: 2307–2312.

27 Reynolds CJ, Pade C, Gibbons JM, *et al.* Prior SARS-CoV-2 infection rescues B and T cell responses to variants after first vaccine dose. *Science* 2021; **372**: 1418–1423.