Upcoming SARS-CoV-2 vaccine: expectations and reality

COVID-19 has created an unprecedented challenge as the world braces itself with the hope that a vaccine can be developed without delay. The crisis has accelerated international response and led to the development of over a hundred SARS-CoV-2 vaccines, of which many are currently under clinical trials. In the absence of a definitive treatment, vaccination possibly remains the most effective alternative to prevent COVID.

The vaccine encoding the SARS-CoV-2 surface spike (S) glycoprotein is mostly chosen as the optimal target for many candidate SARS-CoV-2 vaccines for cumulatively neutralising antibodies and T-cell responses to CoV-2. 1 The measurement of serum neutralising antibody level is considered to be a key correlate of protection; it should ideally correspond to plasma viral neutralising activity and fairly correlate to antiviral immunity. 2, 3 Keeping the past experiences in mind, many issues remain yet to be discussed.

Recent history points to two other coronaviruses, the 2003 SARS and 2012 MERS, for which there are still no effective vaccines available. SARS-CoV-2 is fairly similar to previous SARS-CoV based on phylogenetic analysis, and apparently uses the similar cell entry receptor, largely aimed to stimulate immune response against the viral envelope-protruding spike (S) glycoprotein. Previous experiences with SARS-CoV and MERS-CoV infection have raised the safety issues, particularly vaccine-induced heightened respiratory illness. Severe COVID preserves an immunopathogenic component. The untoward events have been linked to macrophage-tropic coronaviruses vulnerable to antibody-dependent enhancement of replication and can enhance viral entry into human cells and can worsen the disease. Although uncommon, there can be immune complex formation, complement activation, some immunopathologic complications and Th2-biased responses. 4 Ideally, a successful vaccine must strike a balance between protection and excessive immune activation. 3, 5

The dynamic characteristics of antibody responses to SARS-CoV-2 in patients with COVID-19 remain largely unknown, perhaps low titres of neutralising antibody do not result in protective immunity to SARS-CoV-2. Antibodies against SARS-CoV-2 have been seen to be short-lived and wane over time substantially after recovery in convalescent patients with COVID-19. Disappearance of antibodies to SARS-CoV-2 in a patient COVID-19 after recovery has been reported by many patients. 6 Antibody responses to coronaviruses can wane rapidly following infection or immunisation, allowing for potential reinfection, particularly in mild or subclinical disease. Such cases of rapidly declining immunity may allow re-infections analogous to the common cold, coronaviruses. 5

Real-time monitoring of global viral spread suggests that as many as eight strains of SARS-CoV-2 are currently circulating. SARS-CoV-2 isolate genomes have shown to have at least 11 variations in SARS-CoV-2 genome in over 10% of whole isolates from all over the world. Thirty-three unique mutations (six in the S glycoprotein) have been identified, with some variants demonstrating significantly greater cytopathology in Vero E6 cells relative to other viral isolates. 7 A report of 1234 mutations was identified from 12 343 SARS-CoV-2 genome sequences by comparison with the reference SARS-CoV-2 sequence. 8 Consideration of such variations may help in the development of a new vaccine.

Antigenic variation requires constant updating of vaccine formulations. It is needful to monitor genetic variations, a barrier to the development of effective vaccine in respiratory infections like influenza. It is important to recognise the potential signatures of adaptation in SARS-CoV-2. This can also guide the ongoing development of vaccines. 9 The number and frequency of virus point mutations have increased over time. It is also essential to understand if the described mutations could dampen the vaccine outcome and lead to the emergence of drug-resistance viral phenotypes. 10

Traditionally, in standard vaccine trials, high-risk contacts are the target population. Because everyone in any population may not be exposed during the trial and also during follow-up period, so the exposure to infection can vary. This means big trials with extensive follow-up times are essential to accumulate enough cases with exposures to test vaccine efficacy. These vaccine trials are likely to recruit younger individuals, to minimise the risk of adverse effects. Results may not be suitable or equally applicable for older individuals and persons with comorbidities who are likely in most urgent need of a vaccine.

Time will prove a vaccine’s real effectiveness. Even if the vaccine may not be able to prevent infection fully, it might still provide great benefit if it reduces the severity of COVID-19. Some scientific as well as ethical challenges will stand in the process of finding an effective vaccine; however, the efforts must persist and important breakthroughs for mankind must continue.

SARS-CoV-2 has no discrimination for racial, ethnic, economic or national borders. There is a dire need of international coordination, based on the principle of solidarity, for equitable access to COVID vaccine. While equitable access to COVID vaccine remains a big question, another pressing concern is who will assume a leadership role in solving different ethical and administrative issues when WHO is possibly getting sicker in the present scenario.

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