

Foreword

“If the world doesn’t share the vaccine, the virus will take on the world”

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What did George Gao mean by the title quote? The statement certainly feels like a warning, but it is a warning that comes with a prescription that carries optimism and hope.

The warning that the virus will “take on the world” has indeed been the world’s experience during the first year of COVID-19. But the warning is more ominous with the continual emergence of variants of the coronavirus that have differing characteristics – transmission speed, pathogenicity, evasion of immunity to prior infection or immunization (1).

Viruses do not have wants or desires; viruses do not have goals or objectives; and viruses do not have plans for the future. However, viruses are in the realm of the living, they do replicate (with the host’s machinery), and they evolve in directions that favor their continued existence. As long as their continued existence threatens human health, they are taking on the world.

Why should the world’s sharing of vaccines be part of the solution? What contribution can COVID-19 vaccines make? How confident should we be in the ability of vaccines to stop these viruses?

Virus evolution is dependent on mutations that arise during replication in a host that are transmitted to others, creating subtly and sometime not-so-subtly different lineages that can have selective advantage. Stopping replication stops evolution. Preventing infection prevents replication. Preventing transmission prevents infection. To the extent that vaccines are able to decrease the amount of viral replication, viral infection, and viral transmission, the pace of evolution should be able to be slowed, slowing generation of variants, and slowing the virus’ taking on of the world.

Can vaccines do that? The current COVID-19 vaccines have been authorized for use based on their proven ability to prevent clinical disease, not their ability to prevent transmission and infection. However, animal models in preclinical trials showed evidence of prevention of transmission, and evidence is emerging that COVID-19 vaccines prevent infection and transmission. Seeing the large decreases of COVID-19 with widespread use of COVID-19 vaccine in Israel is a good sign with real world evidence (2). We are likely to see more and more evidence that COVID-19 vaccines prevent infection and transmission as the world has more experience with the vaccines.

Based on other routinely-used vaccines, one would expect the COVID-19 vaccines to have some effectiveness against infection and transmission. Look at hepatitis A in China. The number of infections is hundreds of times lower than in the pre-vaccine era after use of hepatitis A vaccines; fewer infections mean fewer replications. Even inactivated poliovirus vaccine (IPV), which is often said to not be effective against infection/transmission, has epidemiologically meaningful effectiveness against infection/transmission (3). Several European countries eliminated polioviruses with IPV alone. Last year, China stopped a three-year-old outbreak of circulating vaccine-derived poliovirus type 2 with Sabin-strain IPV alone (4). These accomplishments would not have been possible without vaccine effectiveness against infection/transmission.

Will vaccines cause selection of vaccine-escape mutants? One would expect that viruses less neutralized by vaccines to have selective advantage over viruses more susceptible to vaccine-induced immunity. However, this is not a reason to not vaccinate. The contribution of selection pressure leading to meaningful vaccine escape is not known. Every year, influenza vaccine is changed in attempt to match the upcoming circulating strains, but the reason that circulating strains change is not from vaccine selection pressure, but rather from genetic drift that happens with or without vaccination.

Virus replication anywhere is a threat everywhere. Not only is ongoing transmission a risk to health where it is happening, but also a risk to other places to which the virus can travel. This is in part the reason for the World Health Organization’s (WHO) call for solidarity in the fight against the COVID-19 pandemic. Along with promoting the development of COVID-19 vaccines, WHO, the Coalition for Epidemic Preparedness, and Gavi created COVAX, a mechanism for sharing vaccines globally. Almost all countries of the world have signed onto

COVAX, and indeed COVAX has already started sharing COVID-19 vaccines (5). Strengthening COVAX with financing and vaccine supports sharing the vaccine with the world.

As George Gao says, sharing vaccines with the world is important to prevent the virus from taking on the world. Vaccines alone, of course, are not enough. Constant vigilance and sensitive surveillance of circulating coronavirus is absolutely essential. The first generation of vaccines may need to be updated to keep up with, and ideally get ahead of virus evolution by finding additional vaccine targets. Population immunity will need to be frequently assessed against circulating strains and tested for waning immunity. Vaccination policies will need to be adjusted as the epidemiology changes.

Ensuring availability and large-scale use of COVID-19 vaccines by all countries, in solidarity against the COVID-19 pandemic, is a vital strategy to prevent the virus from taking on the world.

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