COVID-19 vaccines and appearance of SARS-CoV-2 variants. Reflecting on the case of Mexico

Vacunas contra la COVID-19 y aparición de variantes del SARS-CoV-2. Reflexionando sobre el caso de México

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Blut is ein ganz besonderer Saft.
Goethe

Regarded as one of the most important inventions in human history, vaccines represent the simplest and most cost-effective intervention to protect against epidemics and pandemics. Basically, benefits are related to a reduction of mortality and morbidity, and in turn, include economic benefits by avoiding hospitalization, preventing long-term disability and preserving the economy. However, the development of new vaccines is a highly complex process, since they must undergo extensive review and approval processes by national regulatory agencies before they can be applied to the population.^{1,2} National vaccination programs are also extremely complex in their design, strategy and execution, since they require detailed logistics and a secure supply chain to bring the vaccines to application sites.³

Under normal conditions, a company must invest between 314 million and 2.8 billion dollars (2018 USD) to obtain a new vaccine from the laboratory to the patients.^{4,5} These amounts largely reflect the cost of products that fail in clinical trials and the cost of the time invested in development. Furthermore, it takes between 10 and 15 years for an experimental vaccine to reach the market, and the probability for it to be eventually approved for use in humans is estimated to be lower than 12 %.^{6,7} Companies that produce vaccines are at the forefront of biomedical innovation, which is why they protect their products and processes through solid intellectual property policies that reward

their investment in competitive markets.^{8,9} Thus, countries' public policies are of primary importance for the establishment and development of this sector.

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) appeared in a moment of basic scientific knowledge maturity in some areas, including genomics, structural biology, antigenic cartography and reverse vaccinology. This way, global scientific research could take place at pandemic speed and vaccine development also underwent a paradigm shift.¹⁰ The first complete genome sequence of the virus was released on January 10, 2020 (to date, more than 500,000 sequences are deposited in public and private databases, including 839 sequences from individuals in Mexico). High-income countries quickly generated manufacturing capacity, implemented technologies with novel platforms, obtained licenses for large-scale production, transferred technologies and adapted manufacturing processes.^{11,12} The conduction of clinical trials during the coronavirus disease 2019 (COVID-19) pandemic poses additional challenges, including the way they are conducted and how approval processes occur. Thus, the first vaccine candidate entered clinical trials on March 16, 2020 in the US and, today, there are a dozen licensed vaccines for human use in 64 countries, with more than 5,000 clinical trials registered worldwide.^{13,14} In the midst of the pandemic paradigm, this successful experience of global collaboration to obtain new vaccines (with safety and efficacy attributes in such reduced times) has renewed the discussion regarding a global system for

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the funding, surveillance and allocation of vaccines.¹⁵ In Mexico, this should bring us to a deep reflection regarding the implementation of inter-sectoral public policies on health, intellectual property, science, technology and innovation. Again, we have an opportunity to establish preparedness and response systems for pandemics and health emergencies, which will undoubtedly continue to appear in the future.

The vaccines developed against SARS-CoV-2 largely depend on the induction of antibodies that are able to neutralize it. The emergence of viral lineages with the ability to evade previously assembled immune responses, both in vaccination- and natural infection-acquired immunity, is of special interest for public health.^{16,17} Circulation of these variants of interest puts the developed vaccines efficacy and vaccinated populations protection at risk. Although several groups in the world are already working to modify the vaccines, currently, we do not know if the three variants of interest identified in Mexico (B.1.1.7, P.1 and CAL.20C), and possibly others, represent a risk for approved vaccines (Oxford-AstraZeneca, Pfizer-BioNtech, Sputnik V, CanSino and SinoVac, by March 9, 2021). This requires close viral characterization (by means of novel sequencing, bioinformatics and genomic epidemiology technologies) of the lineages circulating in our country. Given that availability of vaccines is only a first part of the equation, the strategy to achieve coverages that reduce transmission (and thereby the possibility of the appearance of new variants) and implementation of intensive virologic surveillance with well-coordinated epidemiological investigations (inter-ministerial in nature) are urgent challenges for Mexican public health.

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