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# Editorial: mRNA Vaccines and Future Epidemic, Pandemic, and Endemic Zoonotic Virus Infections

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e-mail: [dinah.v.parums@isi-science.com](mailto:dinah.v.parums@isi-science.com)**Abstract**

There have been rapid developments in safe and effective mRNA vaccines for zoonotic infections in the past year. Years of research have made these advances possible, leading to *in vitro*-transcribed (IVT) mRNA expressing therapeutic proteins. There are several advantages of mRNA vaccines that include their low-cost manufacturing process, large-scale and rapid production, and the ability to modify the vaccines in response to emerging infections and viral variants. The COVID-19 pandemic and successful vaccination programs for SARS-CoV-2 have highlighted the advantages of mRNA vaccines. Also, mRNA vaccines are in development for several other potential pandemic zoonotic infections, including Ebola virus, rabies virus, Zika virus, HIV-1, and influenza. There may also be hope for the control of pandemic avian influenza by the combination of improved and rapid viral genotyping and the rapid development and mass production of mRNA vaccines. This Editorial aims to present a brief overview of how mRNA vaccines may help control and future epidemic, pandemic, and endemic zoonotic virus infections.

**Keywords:** mRNA Vaccine • Influenza • COVID-19 • Zoonosis • Epidemic • Pandemic • Editorial

In the 1990s, there was enthusiasm for DNA-based gene therapy to prevent and treat human disease. However, with improvements in mRNA delivery techniques, there have been rapid advances in using *in vitro*-transcribed (IVT) mRNA to express therapeutic proteins [1]. Initial concerns were that mRNA vaccines would be difficult to modify in response to viral variants and would not be as stable as DNA. In 2005, Weissman and Karikó at the University of Pennsylvania identified that the modified nucleotide, pseudouracil, could stabilize the mRNA vaccine [2]. Preclinical studies in animal models showed that IVT mRNA could achieve long-lasting immune responses [3]. Data from early human clinical trials supported RNA-based vaccination as a potential alternative to conventional vaccine production [3].

The advantages of mRNA vaccines include their synthetic nature, the generic and low-cost manufacturing process, the ability for large-scale and rapid production, and the ability to modify the vaccines in response to emerging infections and viral variants [3]. One of the first examples of the practical and rapid development and implementation of an mRNA vaccine was in 2017 during a Zika virus outbreak [4]. Since 2017, the vaccine portfolios of several pharmaceutical companies and biotechnology companies that work with academic institutions have increased.

The COVID-19 pandemic and the development and implementation of vaccine programs to the SARS-CoV-2 virus have

demonstrated the advantages of mRNA vaccines, which have resulted in regulatory authorizations of several vaccines within one year of the onset of the pandemic [5]. Within the first year following the identification of SARS-CoV-2, Pfizer/BioNTech developed the BNT162b2 mRNA vaccine [6]. BNT162b2 is a nucleoside-modified, lipid nanoparticle-formulated mRNA that encodes a stabilized, membrane-bound full-length SARS-CoV-2 spike protein [6]. Emergency use authorization (EUA) for BNT162b2 was given by the US Food and Drug Administration (FDA) on December 11, 2020 [7]. In early 2021, Moderna (Cambridge, MA, USA) published the safety and efficacy data on the mRNA-1273 mRNA vaccine, which received EUA from the FDA on December 18, 2020 [8,9]. It is important to note that BioNTech, Moderna, and others currently have vaccine pipelines to produce mRNA vaccines for several potential pandemic zoonotic infections, including Ebola virus, rabies virus, Zika virus, tuberculosis, HIV-1, and influenza [10].

Avian influenza is a zoonotic viral infection that causes only minor diseases in birds. Currently, seasonal influenza due to influenza A results in between 3 million to 5 million cases of infection and between 300,000 to 650,000 deaths per year [11]. Influenza has resulted in epidemic and pandemic disease for more than a century, with millions of lives lost [12,13]. There have been five major pandemics of influenza variants, including from H1N1 in 1918, H2N2 in 1957, H3N2 in 1968, H1N1 in 1977, and H1N1 in 2009 (H1N1) [12,13]. In 1977, there was

an outbreak of the H5N1 strain in Hong Kong and the H7N9 strain in Southern China in 2013 [14]. Influenza is an endemic zoonotic viral infection that periodically undergoes mutations associated with changes in infectivity and pathogenicity [12]. Influenza variants are managed by public health initiatives and annual vaccination programs [12].

However, the development of viral variants of influenza has occurred at a pace that has been too rapid for effective vaccine development. Of recent concern is new influenza A variants, H10N8 and H7N9 [12]. However, there may be hope for the control of pandemic avian influenza by the combination of improved and rapid viral genotyping and the rapid development and mass production of mRNA vaccines [15]. In 2019, the first phase 1 clinical trials of mRNA vaccines against H10N8 and H7N9 influenza viruses (NCT03076385 and NCT03345043) showed that the vaccines were well tolerated and resulted in humoral immune responses [15].

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The initial response to the epidemic of SARS-CoV-2 was too little and too late and resulted in the pandemic that we currently face [16,17]. This zoonotic virus is now endemic, and just like seasonal influenza, we shall have to 'learn to live with it.' However, living with viruses of high pathogenicity will only be possible with effective vaccination programs.

## Conclusions

New outbreaks from zoonotic viral infections, including from coronaviruses and influenza viruses, require early detection and control to prevent the development of future pandemic and endemic disease. Influenza virus variants and SARS-CoV-2 viral infections are now endemic. The hope lies in rapid and effective vaccination programs that include mRNA vaccine technology.