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Editorial

Vaccines against SARS-Cov-2:

An Unprecedented Scientific Triumph and a Source of Hope in the Pandemic

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Abstract
This article rationalises the culmination of the design, testing, regulatory approval and delivery of the SARS-CoV-2 vaccine in the UK, USA and across the world. The author champions the worldwide collaboration of scientists, industry, governments, regulatory agencies and several thousands of people who have courageously put themselves forward to make this immense feat possible. So that we, the rest of the people may reap the survival benefits. The author presents a balanced view and acknowledges the uncompromising science that has fuelled this marvel- encouraging people who fear the unknown and vaccine sceptics to come forward.

The pandemic of 2020 has changed the world as we knew it. The relentless spread of SARS-CoV-2 through societies has created more misery, destitution and death than any other catastrophes in recent memory. During this pandemic, political cooperation between allies has been rejected in favour of strict border controls to contain the virus. Every nation has sought to protect its own interests - leading to fierce competition in obtaining scarce resources to treat or protect citizens with personal protective equipment, drugs and other amenities. Ironically, some of the worst outcomes during this pandemic have been seen in some of the richest and most advanced Western countries; the reasons for which will be debated and investigated in the years to come.

Despite the political isolation in which most countries have operated, the scientific community has clearly demonstrated its willingness to share knowledge about the virus right from the very outset. Scientific cooperation supported by commercial funding has led to many countries participating in multicentre clinical trials. It was widely expected within the scientific community that a zoonotic coronavirus epidemic was likely to happen [1]. International efforts in pandemic preparedness and vaccine development were stepped up further when the SARS epidemic emerged in the Far East, shortly followed by the Middle Eastern Respiratory Virus (MERS) epidemic in the Middle East, Ebola virus outbreak in West Africa and Zika virus in the Americas. Vaccine development pipelines dealt with pathogen-specific work, platform-based technology such as viral vectors and prototype-pathogen efforts (for example using the West Nile Virus to develop a vaccine that was soon converted to a closely related Flavivirus, Zika virus when the outbreak occurred in the Americas). [2]. Therefore, when within two weeks of identifying a viral outbreak in a wet market in Wuhan, the genetic code of this new zoonotic coronavirus was shared in open resource platforms [3], many scientists understood the potential of this virus to cause a pandemic and set about developing vaccines against SARS-CoV-2 [4].

Scientists have worked round the clock, with the political backing from regulators, financial backing from pharmaceutical industries and the generosity of the common citizen to participate in volunteer trials to bring vaccine development to fruition in an unprecedented pace. This has often vexed critics who have been troubled by the speed at which researchers have conducted the trials and submitted their trial data, often seemingly bypassing the scrutiny of peer reviewed publications. Those in doubt should remember that most of these vaccine developments happened on the back of well-established platforms

that were simply awaiting the scale of funding, the huge numbers of scientists and clinical triallists dedicating their time to vaccine development, the easing of administrative barriers and the sheer volume of participants to make this feat achievable. It is almost as though time travelled horizontally as well as vertically during the last few months.

As of 30th December 2020, according to WHO records, 60 vaccines against COVID-19 are in clinical development and 172 vaccines are in pre-clinical development worldwide [5]. Several technologies are being used in vaccine development – including protein subunit; non-replicating viral vector (VVnr)- for example the vaccine developed by the Oxford group and AstraZeneca and produced in Serum Institute India, licenced in the UK on 30/12/20; DNA; inactivated virus (Bharat Biotech product in India, currently in Phase III studies); RNA (Pfizer-BioNTech product licenced in the UK on 2/12/20 and Moderna vaccines); replicating viral vectors (VVr); virus like particles; live attenuated virus (such as one in collaboration between Codagenix and Serum Institute of India); VVr+ antigen presenting cells (APC) and VVnr+ APC [4].

We now have novel technologies that have demonstrated previously unimaginable success rates in preventing severe illness among infected study participants. For example, the Pfizer mRNA vaccine is reported to confer a 95% protection from developing disease after two doses [6]. The mRNA technology used in the Pfizer -BioNTech and Moderna vaccines, both of which have received FDA approval, has been in development for at least a decade [7]. This has mostly been in the development of cancer vaccines, now deployed with remarkable ingenuity to protect against COVID-19. Lipid nanoparticle-encased mRNA molecules created entirely on a laboratory bench, when injected into a person enters cells and instructs them to make a specific protein within the cytoplasm. Without any involvement of the nucleus, the cell creates new proteins that resemble miniscule parts of the virus- the very parts that are identified by the person's immune cells. The immune cells, completely oblivious to the fact that the protein was manufactured in the cell from an externally obtained 'message', rather than originating from a viral infection, simply turns on its antibody and cellular memory productions, ensuring that protective antibodies are in ready supply when the real virus strikes. The mRNA is degraded using usual cellular mechanisms within days.

The Oxford vaccine group, with funding from AstraZeneca developed another vaccine technology, previously used successfully against the Ebola virus, using a modified virus that causes colds in chimpanzees, but is harmless in humans. These viral 'vectors' are designed to instruct cells to create genetic codes in the nucleus that eventually result in the production of particles that resemble SARS-CoV-2 and deceives the immune system into making antibodies and immune memory cells to protect against COVID-19. The trial was conducted in a huge scale involving thousands of volunteers in 3 countries and demonstrated a relatively modest success rate in preventing severe disease, but still impressive at 65% [8]. Unlike the mRNA vaccine, this vaccine enters the host cell nucleus and instructs the nucleus to make mRNA that eventually results in the development of immunity. Immediate adverse effect of the vaccine is somewhat more pronounced than the mRNA vaccine, but limited to reactions such as fever, fatigue and arm pain.

Throughout the pandemic, governments have faced a difficult choice between curbing personal liberties and economic activity versus allowing the virus to spread wildly within populations. Some countries followed the former strategy while others, the latter. Those with severe lockdowns managed to 'flatten the curve'- delay the peak infection rates until health systems had the opportunity to expand to cope with the inevitable spread once the lockdowns were lifted. Add to that the serious concerns about viral mutations, as is currently being seen in the UK, where a virulent strain has spread despite significant restrictions [9]. In this scenario, widespread vaccination is the only hope to protect citizens from developing severe illness, filling up hospital beds and destroying families and economies.

Several vaccines are likely to be available for general use in due course. Mucosal immunity obtained via nasal administration of vaccine might prevent viral entry to the respiratory tract in the first place. It is likely that combination of vaccines will be used, and some vaccines that are logistically less challenging to administer will be used in more people across the world. It remains to be seen whether SARS-CoV-2 continues to mutate every year, resulting in the need for 'tweaking' vaccine production methods to match the viral strains.

The pandemic has been fraught with misinformation, conspiracy theories and vaccine scepticism [10]. Whilst vaccine scepticism has been prevalent since the time the first ever vaccines were developed [11], the democratisation of opinion via social media in recent years, have driven it to the mainstream. The pandemic has seen some of the most worrying misinformation attain epidemic proportions [12].

It is well established that in Western countries, COVID-19 has disproportionally affected people from Black and minority ethnic backgrounds, reflecting inherent inequalities and unfairness that exists in society. Some of this may have perhaps resulted in the lack of trust that certain disadvantaged groups feel towards the speed of regulatory approval that has been granted to vaccines and the governmental push to get mass vaccination implemented to obtain herd immunity. Digital media is filled with thousands of healthcare professionals and healthcare organisations keen to demonstrate 'leading by example' of how vital and safe the vaccine is. Paradoxically, the very people who are at a disadvantage (due to the unfairness in society or their own co-morbidities) are likely to be the victims of vaccine scepticism and therefore choose to decline the offer of the life-saving vaccine.

It will be important to remember that COVID-19 has thus far infected a staggering 80 million people worldwide, of whom 1.7 million have succumbed to the disease [13]. The benefit conferred by the two approved vaccines in the UK, now trialled in over 40,000 human volunteers will far outweigh any minor short- term discomfort or even concerns regarding long term safety of novel vaccine platforms. COVID-19 has wrecked families, livelihoods and lives - including the indirect health effect of the pandemic with delayed presentation with non-communicable diseases, maternal health, mental health, routine surgery, treatment of chronic diseases and other communicable diseases such as HIV/AIDS and malaria. There is also no doubt that any healthcare worker who has faced the virus will be first in line for the vaccine.

Vaccines have allowed humanity to achieve its scientific, economic and material prosperity such as those we enjoy in modern times. The COVID-19 vaccine is our ticket out of this nightmare that has completely changed the way we live and interact with others. COVID-19 is here to stay. A vaccine will allow us to keep it in bay, so we can think of a future that does not involve social isolation and financial destitution.

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