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REVIEW ARTICLE

A Review on Vaccine Development Strategies Against Emerging Pathogens: COVID-19 Experience

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ABSTRACT

Background: There may be some mutually useful lessons to be learned by comparing the vaccine methods and technical platforms utilized for the COVID-19 pandemic to those used for earlier emerging (like HIV infections, SARS, Lyme disease, dengue fever, West Nile virus, and the Zika virus)and re-emerging (including malaria, tuberculosis, cholera, pertussis, influenza, pneumococcal disease, and gonorrhea) infectious illnesses and pandemics.

Objective: Regulators, health authorities, and political constituencies all face considerable challenges as a result of the enormous breadth and rapidity of the development of contemporary infectious diseases. Vaccine manufacture and delivery are challenging and complex processes. Together with speed, other important factors include pharmacovigilance of vaccination safety, tracking of virus changes, and clinical development to emergency use authorization and license. The importance of vaccine access must be prioritized in low- and middle-income countries.

Results: The result of efforts to halt the current and any prospective pandemics of infectious illnesses will be greatly influenced by the total of these factors.

Keywords: COVID-19, Vaccine, pandemic, Contagious viral diseases

INTRODUCTION

Contagious viral diseases have repeatedly emerged and posed a threat to humanity throughout history. All forms of transportation, large gatherings, changes in human social behaviour, environmental changes, and a lack of global public health initiatives all contribute to modernization's high mobility. Animal diseases are now threatening to wipe out humans because of how quickly they propagate. At the time, the population of the world was estimated to be around 1.8 billion. By 2050, more than one fourth of the population of the world is predicted to have increased to 9.9 billion, up from 7.8 billion todays. Over 1.8 billion people were thought to be living on Earth at the time. The world's population is expected to expand by more than one-fourth by 2050, from 7.8 billion people today to 9.9 billion. With only six months to spread the virus, the COVID-19 pandemic [1-3] killed many elderly people and people with pre-existing medical issues, especially those with chronic illnesses. The entire economy has been devastated by this pandemic. Lockdowns have been replaced with more stringent and unsuccessful prevention measures such as self-distancing, masking, travel bans, and avoiding gatherings. The global Ebola outbreak, which has infected and killed more than 100 million people, appears to be manageable with the help of current

interventions and immunization alternatives. Researchers therefore must re-evaluate how they monitor and handle dangers from newly emerging infectious diseases while also improving mechanisms for managing pandemic illness globally [4,5].

Increased prevalence of infectious illnesses

Since the beginning of time, new infectious diseases have been identified without the fundamental infectious agents being discovered [6,7]. Despite the development of antibiotics, globalization and interconnection have made it harder to contain infectious diseases, Emerging infectious diseases (EIDs) still pose a significant threat to public health worldwide. Pandemic disease history may be traced back to the SARS-CoV-2 pandemic and previous Coronavirus outbreaks. [8,9] Infectious organisms will be able to colonize the ecological niches that human civilizations generate as they grow in size and complexity. Communities are constantly at risk of new and re-emerging diseases, as well as their variable capacity to rapidly erupt into pandemics and epidemics. This is indicated in Table **1.**

Table 1. Distribution of Infectious Diseases and Mortalities

	Infectious diseases	**Mortality**
Year 1918	Spanish flu	Between around 50 million and 100 million
Year 1931	Rift Valley Fever	CFR of 1% overall; 50% with hemorrhagic fever
Year 1937	West Nile fever	5% CFR
Year 1967	Marburg hemorrhagic fever	Mosquito-borne; most recent worldwide epidemics (U.S.A., 1999–2010)
Year 1969	Lassa fever	5,000 fatalities every year; CFR 1-2 percent; Nigerian CFR 25%
Year 1969	Acute hemorrhagic conjunctivitis	Rare
Year 1976 to 2020	Ebola hemorrhagic fever	More than 15,000; CFR 75%
Year 1981	HIV/AIDS	Approx.37 million
Year 1996	Avian flu	Extremely High Case fatality Ratings (60 percent)
Year 1999	Nipah fever	Less than 1,000; extremely high case fatality rate
Year 2002	SARS	803, and the CFR is less than ten percent
Year 2009	Swine Flu	284,000 people; CFR ranging from 2.9 to 9%
Year 2012	MERS	935; Case fatality rate estimated was 34.4%
Year 2014	Chikungunya	Was rare
Year 2015	Zika	Was unknown
Year 2019–ongoing	COVID-19 (SARS-CoV-2)	Greater than 2.3 million; Case fatality rate ranging from 2 to 10%.
CFR, case-fatality rate.		

Yellow fever and dengue fever are two more viruses spread by mosquitos that are not mentioned in Table **1**. Yellow fever has been endemic in over forty countries in Africa and Latin America for decades. Since 2016, Angola, the Democratic Republic of the Congo, Nigeria, and Brazil have all seen yellow fever outbreaks, raising severe concerns about vaccine supply. All live attenuated vaccines developed from the 17D live attenuated yellow fever strain have been shortlisted and prequalified by the World Health Organization (WHO) [10].

In the majority of dengue-endemic areas, the four dengue virus strains (DENV1–4) coexist, posing a significant risk to global public health. Dengue infections and illnesses have increased in recent years as a result of population growth, the proliferation of *Aedes mosquito* species, and the ease with which travellers can move [11]. Dengue fever is a mosquito-borne disease that can be transmitted in over a hundred countries. Dengue sickness is estimated to infect 400 million people each year. Dengue fever is estimated to kill 22,000 people each year and infect 100 million people worldwide. Infections spreading from the Americas and Southeast Asia are wreaking havoc in the Western Pacific, with the region bearing 70% of the Global Burden of Disease (GBD) (https://www.cdc.gov/dengue) [12,13]. Several vaccinations have been developed, including those for Hepatitis and Influenza, Measles, Mumps, Rubella, Diphtheria, Tetanus, and Pertussis. Despite having low acceptability, Dengvaxia, a Sanofi Pasteur dengue vaccine, has been authorised in 20 countries. A safety signal in dengue-seronegative vaccination recipients ignited a discussion in the Philippines that involves the government, regulatory authorities, Sanofi Pasteur, doctors in charge of testing and administering the vaccine, and parents of children who had received the vaccine. These events all resulted from an international examination of the vaccine performance profile, new WHO proposals for usage, and an evaluation of the vaccine performance profile [14].

Both of these bacterial infections frequently generate outbreaks and are growing increasingly resistant to therapy. Since 1817, the sixth global cholera outbreak began in 1961[15]. The outbreak was driven by pathogenic Vibrio cholerae strains. Due to the cholera pandemic, tetracycline, chloramphenicol, sulfamethoxazole, furazolidone, trimethoprim-nalidixic acid, and fluoroquinolones have all been delayed. Numerous vaccines have been prequalified by the WHO, resulting in a Gavi-funded global stockpile that can be promptly distributed in the event of an outbreak. Salmonella enterica serovar Ty is one of the bacteria that cause typhoid fever (S. Typhi) [16,17]. Antibiotic-resistant strains of *S. Typhi* are becoming more frequent. The first large-scale development and transmission of an XDR *S. Typhi* clone have been recorded in Sindh, Pakistan.Each year, cholera kills between 21,000 and 143,000 people, primarily in Asia and Africa, where an estimated 1.4 million to 4.3 million cases have been documented. Epidemics have wreaked havoc in Yemen and Haiti [18]. Antibiotics and rehydration therapy have both been used to decrease the duration of diarrhoea and halt the spread of bacteria. Throughout Asia and Africa, a variety of medications, including chloramphenicol and fluoroquinolones, have developed resistance to antimicrobials. With the assistance of Gavi, the WHO has built a worldwide stockpile of vaccines that can be promptly distributed in the case of an outbreak. Salmonella enterica serovar Ty is one of the bacteria that cause typhoid fever. Antibiotic-resistant strains of *S. Typhi* are becoming more frequent. Since they initially appeared in Pakistan's Sindh region, outbreaks of XDR S. Typhi clones have increased in India, Bangladesh, Nepal, Iraq, and Guatemala [19,20]. The fast spread of S. Typhi in densely populated areas has brought global events to a head. Typhoid strains with increased toxicity demand the development and application of more immunogenic and effective vaccines (conjugation of the Vi polysaccharide with a carrier protein) [21,22].

Infectious disease serves as an excellent model for vaccine development

How we might interpret emerging infectious diseases arising has progressed essentially throughout the most recent twenty years. Despite the fact that the SARS-CoV epidemic in 2002 resulted in a negligible mortality and infections, the disease's lethality and spread caused significant global disruption (see Table **1**). It came to an end with the development of vaccinations. The disease has not resurfaced since then as a result of the closure of wet markets and the eradication of civet-to-human transmission. As a result, funding in order to develop SARS-CoV vaccine was cut in half, and the research was shelved. Only two vaccinations were evaluated in phase 1 clinical

trials: a DNA vaccine 24 and an inactivated vaccine [23]. So, it is highly recommended that the vaccine must go through the next phases and should complete it proper trails.

In a typical R&D pipeline, it typically takes five to ten years to develop a vaccine against an infectious pathogen [24]. When a new disease emerges in the midst of an epidemic, this technique is ruled out. The 2014 Ebola epidemic in West Africa is depicted in Figure **1**, as are the dates and epidemic curves for the COVID-19 vaccine. The 2014 Ebola outbreak claimed 11,325 lives. During this time period, Ebola vaccines were developed and tested, with the efficacy of one vaccine determined after the outbreak ended [25,26]. Quick research, analysis and development enabled the COVID-19 pandemic to achieve interim vaccine effectiveness evaluations in less than 300 days [27], establishing it as a model of rapid research and development. The World Health Organization (WHO) recommended expediting the development and evaluation of candidate vaccines in response to concerns about Ebola's unchecked spread in Western Africa. Gavi negotiated an advance purchase agreement with manufacturers to ensure that the Ebola vaccine would be manufactured and distributed. However, throughout the outbreak, there were previously created Ebola vaccines that were deemed unsuitable for human testing or commercial development [28].

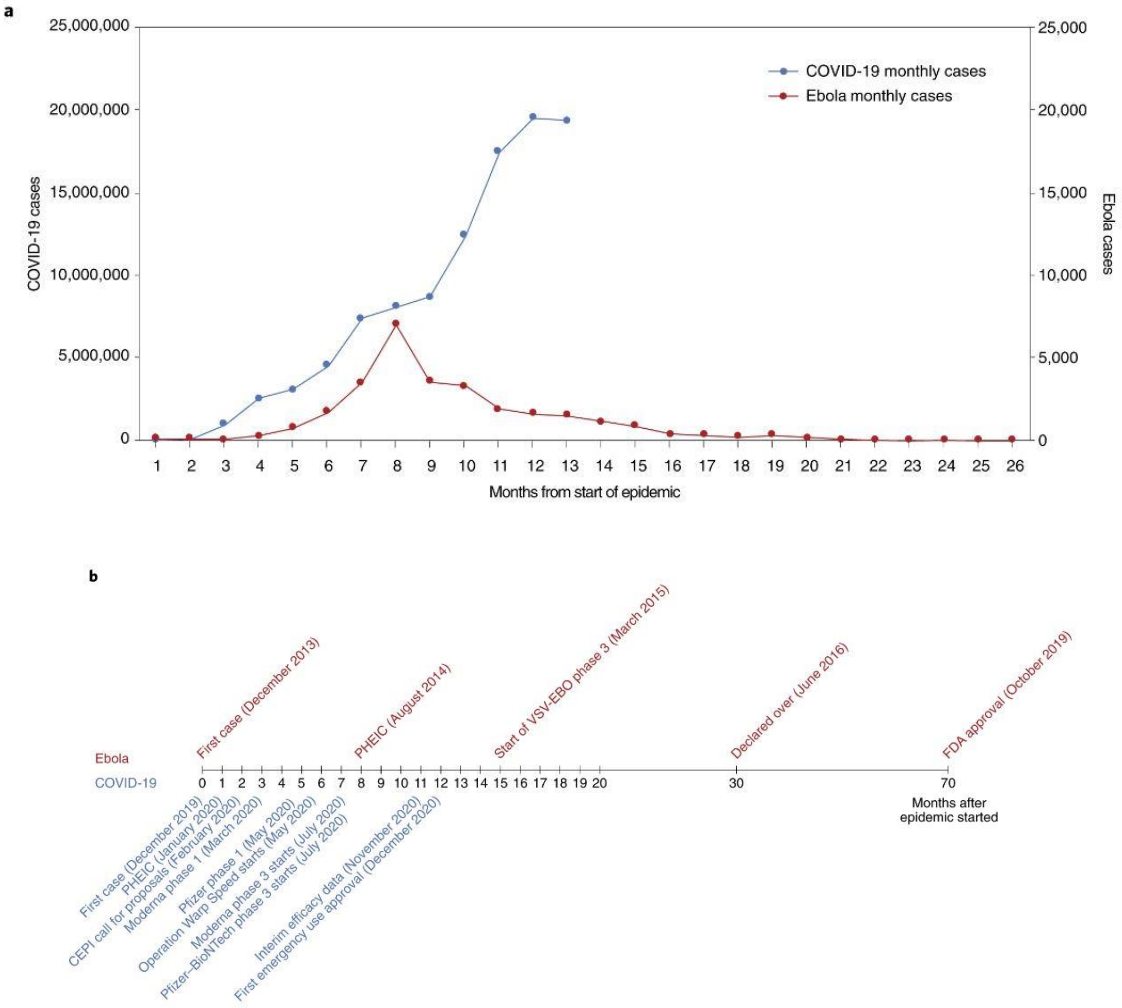

Figure 1. The development of the COVID-19 vaccine and 2014 West African Ebola outbreak and are depicted.

a, the number of cases reported each day during the pandemic is shown against the number of months since the outbreak began. The Ebola axis is on the right, while the COVID-19 axis is on the left.

b, The COVID-19 and Ebola vaccine development schedules in light of the epidemics' distinct happenings. PHEIC is an acronym for "public health emergency of international concern" (PHEIC).

To address these alleged constraints on the production of vaccines during public health emergencies, CEPI (Coalition for Epidemic Preparedness Innovations) was established as a non-profit organisation. Initially, CEPI concentrated on Chikungunya, Nipah, Lassa fever, Rift Valley fever (RVF), and MERS [29,30]. CEPI's responsibilities included the preparation of vaccine stocks for potential usage in the case of an outbreak. Additionally, CEPI has made preparations for "disease X" by putting funds into new platforms for quick responsesuch as mRNA and DNA technologies that instead of taking months or years, might hasten the process of going from the sequencing to the clinical trials by a few weeks. These platforms proved useful, when in January 2020 COVID-19 was proclaimed a pandemic and a worldwide public health emergency in March 2020 [31,32].

CEPI has aided in the development and production of vaccines by Moderna, Inovio, Oxford–AstraZeneca, and Novavax. Due to these organizations' up-front financial commitments, vaccine innovators face less financial risk, which has hastened the development of vaccine concepts into clinical trials while also assisting in the establishment of scalable manufacturing techniques. Operation Warp Speed [33], a larger, US-funded effort, gave additional cash to firms, mitigating the danger of hasty vaccine development and enabling them to meet their initial vaccination dosage pledges.

Frameworks for the development of new infectious disease medications and vaccines that are already accessible

When it comes to avoiding pandemics and epidemics, immunization is unmatched and by promptly administering, a vaccine can assist in containing an outbreak. As previously stated, the standard vaccine development cycle is unsuitable for pandemic requirements. New vaccination platform technologies have the potential to shorten this cycle by enabling the development, testing, and production of many vaccines [34]. Table **2** summarizes several of the most significant technical platforms for developing vaccines against viral infectious diseases that have been developed or are in development. Pfizer–BioNTech [35] and Moderna [36], both mRNA-based COVID-19 vaccines, have been given emergency use licenses by the US Food and Drug Administration (FDA) [37,38], while the European Medicines Agency has granted provisional marketing authorization (EMA) [39,40]. At this stage, declaring mRNA vaccines to be a universal vaccine approach for EIDs is premature (such as bacterial or enteric pathogens). Despite the fact that the COVID-19 mRNA vaccines are excellent evidence of concept, learning from their widespread use and effectiveness studies will take time and effort.

Despite the fact that DNA vaccines for animal use have been approved and have demonstrated safety and ability to elicit an immune response (immunogenicity) in clinical studies involving humans, no DNA vaccine has been licensed for human use[41]. Adjuvants added to recombinant proteins significantly retard pathogen development (for example, subunits, virus-like particles). Vaccines against human papillomavirus and hepatitis B based on virus-like particles are easy to create in large quantities, are safe, and are immunogenic. Additionally, it may be carried with you wherever you go. Every pathogen, whether inactivated or live attenuated (e.g., SARS-CoV-2, polio, or cholera), has a vaccine (e.g., SARS-CoV-2, polio, chikungunya). Biosafety level 3 vaccines, such as the COVID-19 and polio vaccines, may be difficult to transport, limiting their utility in increasing global vaccine production capacity.

Additionally, non-replicating vectors, live, attenuated vectors, or vectors that do not replicate can be utilised. Examples include the human adenovirus ChAdOx and the chimpanzee adenovirus MVA. The condition being treated may be represented by a single insert or by several inserts combined into a single vector. The Ebola vaccine from Merck is a prime example. We replaced the G protein of the VSV vaccine with encapsulated Zaire Ebolavirus envelope glycoprotein. The FDA and EMA have classified VSV's ERVEBO as an excellent "platform" for COVID-19 and maybe future EID vaccines26, making it an alluring "platform," despite the difficulty of maintaining an ultracold chain at -70 °C. Speed of development, simplicity of scaling up production, logistics (display and storage conditions, as well as administration), knowledge transfer to other producers to ensure a global supply, and product price are all important considerations when creating new products. Ad5, Ad26, and MVA42 have been used as virus vectors in the development of HIV and Ebola vaccines. Finally, regulatory agencies rather than platforms approve vaccinations. Vaccines are a world-first. A more expedited evaluation and clearance process may be achievable if regulators have greater confidence in

the vaccine platform's overall safety and efficacy during a pandemic. COVID-19 proposes that if authorities may expedite their evaluation of "platform" technologies like DNA and RNA that have already been used (for other purposes) in conjunction with hundreds of people's safety profiles.

Both the HIV44 and Ebola [42] vaccines have been extensively studied in terms of HPB (heterologous prime–boost) immunization. COVID-19 is now being evaluated against three vaccines: AZD1222, Gamaleya Sputnik V, and Pfizer–BioNTech. Additional HPB vaccine combinations based on mRNA, DNA, viral vectors, and proteins may be taken into consideration. It is feasible to avoid multiple dose reactions and anti-vector side effects while enhancing the immune response. Additional vaccines may be given to individuals who have already completed the standard immunization programme (single or two doses, for example). As a result, immunizations may be less necessary in developing countries (LMICs). Clinical studies and evaluations of implementation challenges should be used to assist producers, funders, and regulators in gaining a better understanding of the whole spectrum of HPB potential [43].

Vaccine labelling should be consistent to make tracking their shelf life easier. This can be accomplished by adopting a no-fault approach for serious vaccine-related adverse events, three-dimensional bar coding, standard indemnification and liability language, and regulatory oversight based on the date of manufacture rather than the date of expiration [44,45].

The procedure for obtaining EUA certification, licensure, and other obligations

Because to organisations like CEPI and programmes like Operation Warp Speed, businesses in the pharmaceutical and biotechnology industries have conducted effectiveness trials in nations or regions with the highest SARS-CoV-2 incidence rates. According to their pledges, the same organisations will fund a large-scale production. The results of randomised clinical effectiveness studies with clinical endpoints may not be sufficient to grant EUA and licencing to vaccine candidates not included in the initial wave of testing and approvals, in addition to the 60 vaccine candidates now undergoing clinical trials and the extra 170 vaccine candidates in preclinical development. (Map of WHO COVID-19 vaccine) [46]. Clinical research comparing noninferiority to vaccines with demonstrated clinical efficacy may be required to obtain additional regulatory and ethical clearances. Investigations are being done on a vaccination that has been clinically proven to work as well as a novel vaccine that produces the same immune reactions. To what extent are regulatory authorities willing to accept bridging studies [47] as a substitute for clinical endpoints? To accomplish so, scientists will need to agree on ICPs against COVID-19. Not all vaccinations, whether proteins or fully inactivated virus, have the same immunological impact. Is it conceivable, for example, for ICP to disseminate uniformly across multiple vaccine platforms?

When sickness incidence rates decline as a result of long-term mitigation and vaccination activities, larger sample sizes, longer participant accrual periods, and more sophisticated logistics are anticipated. As long as a firm commitment to blinding participants in ongoing and future placebo-controlled trials exists, immunizations can be rapidly implemented through emergency use lists (EULs) or equivalent regulatory mechanisms [48].

The population-level protective benefit of vaccination may be exaggerated in randomized controlled trials. The disease will not spread to anyone who come into contact with those who have not got the COVID-19 vaccine. Also, people who have received the vaccine will be less likely to contract the illness from those who have [49]. The importance of vaccine-induced herd immunity in establishing the vaccine's public health value would be missed by research using random assignment and disregarding geographic dispersion.. Additionally, a range of clinical study designs have been proposed to evaluate the efficacy of COVID-19 vaccinations, including the amount of protection conferred to vaccinated and unvaccinated persons in certain populations50, following the current phase 3 trials [50].

It is unknown how much ICP will be employed in future effectiveness trials for the COVID-19 pandemic. Clinical endpoints are more predictive of ultimate clinical outcomes when ICP is used in inferential analysis. Without a complete understanding of viral pathophysiology and immunity, it will be impossible to design vaccines to avoid future outbreaks. This research should also help our knowledge of the immune system's reduction in effectiveness at protecting us from illness. Demonstrating these associations is getting more difficult as vaccine efficacy improves, as there may be

insufficient sick vaccination recipients to compare to uninfected recipients. If the vaccine effectiveness in the clinical trial is less than 50%, ICP analysis may be achievable. The risks of vaccine-associated respiratory disease and the vaccines' long-term safety were not assessed [51].

Pharmaceutical surveillance and pharmacovigilance

CoVID-19 vaccine pharmacovigilance preparations were discussed at the 42nd global advisory committee conference in May 2020. According to the speakers, all countries should be prepared to conduct COVID-19 vaccine safety surveillance prior to initiating any injections. Covid-19, a WHO guideline for vaccine safety surveillance, details the protocols for reporting, monitoring, and documenting any adverse reactions to vaccination [52]. Additionally, it emphasizes the importance of doing follow-up studies once immunizations are licensed to ensure their safety. When it comesto surveillance, the duration of the monitoring is critical. Local, national, regional, and global surveillance must be coordinated. Although nations should incorporate WHO recommendations into their overall plans for the introduction of vaccines, the COVID-19 Vaccines for Global Access (COVAX) initiative, which is coordinated by CEPI, Gavi, the Global Vaccine Alliance, and WHO, must work with partners on capacity building and practical implementation aspects, offering specialised technical and training support [53].

The EMA and national competent authorities in EU member states have created COVID-19 vaccine-specific pharmacovigilance policies in light of the public health emergency and the massive vaccination programmes planned worldwide. Good pharmacovigilance practices include guidelines and standards for risk management plans (RMPs) and immunization mandates. The COVID-19 vaccine's basic RMP criteria were developed to standardize the preparation of these plans by firms and their approval by third parties [54]. The RMP was prepared to assist marketing authorization holders in preparing post-authorization safety surveillance for COVID-19 vaccines. The COVID-19 Safety Technical Working Group was established by the ACIP's Committee on Immunization Practices (ACIP) in June 2020 to provide guidance to the COVID-19 Vaccine Workgroup and the ACIP as a whole about vaccine safety monitoring during development and post-approval pharmacovigilance [55].

The development of new vaccinations can tell us a great deal about how to respond to epidemics and pandemics. Only a few countries are believed to have been adequately prepared for the 2009 H1N1 flu outbreak, which included extensive vaccinations and meticulous monitoring of potential adverse results. The African Vaccine Regulatory Forum [56] investigated vaccine approval and implementation. Such models can be used to guide pharmacovigilance for COVID-19 vaccination in low-resource LMICs. Despite the absence of a worldwide public health emergency, the launch of the first licensed dengue vaccine yielded valuable insights for vaccine pharmacovigilance, including the discovery of vaccination-associated increased sickness [13,14]. ADE and vaccine-associated respiratory sickness have been recorded as a result of the SARS-like CoV-2's sequence similarity to the SARS-CoV, raising possible safety concerns (VAERD). VAERD or ADE are not mentioned in the most recent phase 3 investigations of the SARS-CoV-2 vaccine. VAERD was not detected in animal challenge testing using protective vaccinations against the SARS-CoV-2 virus [50]. There are still unanswered uncertainties regarding the effect of immunizations (or diseases) on antibody titers, emphasizing the critical nature of routine testing [57,58].

Pregnant women are especially vulnerable to disease outbreaks and pandemics [59,60]. Pregnant women's interests should be considered in the development and deployment of vaccinations against developing illnesses, according to the Pregnancy Research Ethics for Vaccinations, Epidemics, and New Technologies Working Group (PREVENT) [61,62].

It is also crucial to monitor the spread of SARS-CoV-2 and other coronaviruses (MERS, seasonal) [63]. Researchers worldwide are discovering new SARS-CoV-2 versions of the virus. D614G has already overtaken the dominant allele in a number of populations [64–66] due to its increased transmission in microscopic animals and faster in vitro growth. In the United Kingdom [67] and Brazil [68], different levels of worry have been expressed in relation to enhanced transmission capacity and, potentially, death. The occurrence of N501Y in South Africa and the improved ability of N501Y to bind to the human ACE2 receptor strongly suggest that N501Y is more easily transferred. As of the second half of 2020, South Africa's B.1.351 strain possesses nine spike mutations and is resistant to neutralizing antibodies

induced by infection or vaccination with previously described influenza viruses. Recently, South Africa prohibited the AstraZeneca COVID-19 vaccine due to its ineffectiveness against B.1.351, which accounts for 90% of all cases in the country [69-70]. Novavax [71] protects against 86 percent of UK variants and 60% of South African variants. Johnson & Johnson's Ad26 is 57 percent effective against mild to severe COVID-19 infection, according to South African researchers.

Immunity to SARS-CoV-2 may have developed in previously infected individuals, while vaccine-induced cell-mediated immune responses may help minimize the risk of infection with new variants such as B.1.351. Nobody knows how vaccine-induced immunological pressure impacts virus proliferation or how changes in vaccination schedule or dose affect virus evolution. Vaccines against strains present in the United Kingdom and Brazil, for example, may become ineffective in the future [72]. As with influenza, surveillance for COVID-19 in humans and animals will need to be strengthened. Global influenza surveillance has been the responsibility of the World Health Organization's Global Influenza Surveillance and Response System since 1952. The Global Influenza Surveillance and Response System enables tracking of influenza viruses and other respiratory ailments on a global scale, as well as serving as an early warning system for novel strains and pandemics [73]. The Global Initiative for Sharing Avian Influenza Data (GISAID) (https://www.gisaid.org) enables quick sharing of data on all influenza viruses, including the COVID-19-causing coronavirus. Along with the genetic sequences of avian and other animal viruses, this dataset contains clinical and epidemiological data, geographic information, and species-specific information. Ebola and all other EIDs, particularly those that are most fatal and spread rapidly, should be included in molecular epidemiology surveillance. As with influenza vaccine research, SARS-CoV-2 vaccine development must be proactive, as platforms such as mRNA can rapidly generate novel vaccine strains. Regulations governing strain alteration must be discussed by the appropriate authorities.

Accelerating the licensing and EUA approval processes carries hazards

Historically, vaccines have been authorized by national regulatory authorities such as the US Food and Drug Administration or the European Medicines Agency (EMA). After getting clearance from a country's strict or effective national regulatory authority, a manufacturing business may apply for WHO prequalification. WHO does not require prequalification of SARS-CoV-2 vaccinations intended for COVAX prior to their first use. When the WHO, the European Commission, and France launched the Accelerator for Access to COVID-19 Tools in April 2020, COVAX was one of three pillars. UNICEF benefits from WHO EUL-certified immunizations as the Vaccine Alliance's largest user. AMC (https://www.gavi.org) or one of the 98 self-financing countries is the only means to obtain vaccines for the 92 low- and middle-income countries (LMICs)[k] [74].

The FDA has approved the first use of vaccines from Pfizer, Moderna, and Johnson & Johnson under the EUA process during this current pandemic emergency. They are using a process known as "conditional approval," according to the European Medicines Agency (EMA). The WHO created the emergency use assessment and listing (EUAL) approach in response to the Ebola virus outbreak in Africa [75]. EUAL was designed to provide guidance to national regulatory bodies in circumstances where "society is willing to accept less trust in the efficacy and safety of products." The WHO will release a new EUL approach in early 2020 to decide whether the quality, safety, and effectiveness of a vaccination are acceptable and whether the benefits outweigh any anticipated risks or uncertainties. Vaccines licensed by EUAL will eventually be reviewed and prequalified. WHO members can use the EUL approach to authorize the use of unlicensed immunizations in their countries [76].

Several countries have established their own regulatory agencies to assure the approval of vaccines developed in their own country. Sputnik V COVID-19 vaccine, developed by Gamaleya Research Institute and based on Ad26 and Ad5, has been licensed for use in adults aged 60 and over in Russia [77-79]. China's National Medical Products Agency, an 80 percent subsidiary of Sinopharm, has granted provisional approval for the complete inactivated virus BBIBP-CorV COVID-19 vaccine. The vaccine is now available to the general public, following the company's announcement that phase 3 trials demonstrated an efficacy of 79 percent [80]. Although the initial results have not been publicized, they must have been assessed and approved by the Chinese Center for Disease Control and Prevention

(CDCP) and the National Medical Products Agency (NMPA). On the basis of preliminary analysis data, the United Arab Emirates became the first country to approve the Sinopharm vaccine for EUA in early December 2020 [81]. Sinovac CoronaVac vaccine has been granted provisional approval based on preliminary efficacy results. Clinical trials have demonstrated that vaccination against CanSino BIO COVID-19 is 65.7% effective in avoiding symptoms (unpublished). The intermediate experiment with vaccines was 90 percent effective in preventing serious illness [82,83]. In Mexico and Pakistan, the vaccine was delivered as an EUA [84].

Increased production and increased efficiency are crucial in the industrial sector

Despite a lengthy and difficult manufacturing procedure, the COVID-19 vaccine was developed and made available to the public within a year of the virus's discovery. Numerous criteria are considered while determining the safety and efficacy of a vaccine, including the vaccine's technical platform, dosage, schedule, manufacturer capability, and reputation (mRNA, fully inactivated virus, vector, and protein with or without adjuvant). Industrial scale-up in its early stages will have a considerable effect on vaccination supply [85]. Vaccine nationalism, as well as new bilateral deals between vaccine makers and rich countries, may play an impact. To meet expanding demand from China and India, they'll need to leverage their huge manufacturing capabilities. Certain COVID-19 vaccines manufactured in the West85 and China86 have already been delayed [86].

DCVMN (Developing Countries Vaccine Manufacturers Network) was founded in 2000 with the mission of procuring and distributing low-cost vaccinations for both established and newly emerging infectious disease threats. According to DCVMN members 88, DCVMN members manufacture 70% of EPI immunizations and 75% of vaccines supplied by the United Nations [87]. Transfers of technology to DCVMN members have had a significant impact on global health in recent decades. As part of the DCVMN, the International Vaccine Institute transferred vaccine technology developed in Vietnam to VABIOTECH and other DCVMN partners, including ShanthaBiotechnics (Shanchol) in India, EuBiologics (Euvichol) in the Republic of Korea, and Incepta (Cholvax) in Bangladesh. Only Bangladesh has access to Cholvax, a WHO-approved medicine that is a major contribution to Gavi16's global stockpile [88].

The Serum Institute (India) and SK Bioscience (Korea) have licensed or contracted AstraZeneca and Novavax to manufacture COVID-19 vaccines, while Moderna has licensed or contracted Johnson & Johnson and Lonza (Switzerland) to manufacture COVID-19 vaccines, and Chinese Sinovac has licensed or contracted Johnson & Johnson and Lonza (Switzerland) to manufacture COVID-19 vaccines (Indonesia). License and contract manufacturing agreements are intended to result in the production of sufficient vaccine doses to be distributed to vulnerable population worldwide [89].

Due to the pandemic's urgency, proof of concept for the COVID-19 vaccine is more crucial than addressing other practical challenges such as vaccine installation, supply, and dose. Neither the COVID-19 mRNA vaccine nor Merck's VSV-EBO Ebola vaccine can be stored in an ultracold chain. When it comes to universal immunization, the scalability of these technologies remains an unresolved subject. It is necessary to conduct extensive research on vaccination stability in hot conditions (Pfizer mRNA). According to published data, the COVID-19 and other EID vaccines may provide some protection following the initial dosage [90].

As a result, vaccine and other therapy distribution, skewed

Priority is given to low-income nations in the 2030 Agenda for Sustainable Development to ensure that no one is left behind. COVID-19 has experienced both ends of the spectrum of exceptionality. By the end of 2021, a minimum of 2 billion doses of WHO-approved vaccine will be distributed to participating nations, covering about 20% of each country's immunization requirements. Gavi [90] intended to deploy AMCs to administer vaccinations in 92 low- and middle-income countries. The United States appears to be joining COVAX in meeting its 50-dose target for 2021, which the business stated earlier this month that it has purchased sufficient doses to meet [91].

Vaccinating people in low- and middle-income nations will cost billions of dollars. In terms of the global economy, this investment appears to be sound. Although no AMC countries have been vaccinated, COVAX is on schedule and prepared to commence vaccine distribution; millions of people in high-income countries have already been immunized. Preordered dosages outnumber the population by an order of magnitude in high-income countries. What are the

possibilities that COVAX will be able to reach its 2 billion dosage targets by 2021, or will manufacturing issues result in a pandemic extension and spread to impoverished countries? If they do not receive COVID-19 vaccines, this will be practically impossible for low-income countries, who are already struggling with poverty and inequality as a result of the current epidemic [90].

He believes that all children should be vaccinated against COVID-19. Fear of vaccines impedes global recovery [92]. It has been demonstrated that if the first two billion doses of COVID-19 vaccine are delivered in an inequitable manner, the disease's global death toll will increase. COVAX will ensure that COVID-19 vaccines are made available to all countries in a timely and equitable manner.

CONCLUDING REMARKS

The insights learnt from the COVID-19 outbreak should be incorporated into new vaccines against emerging infectious diseases and pandemic pathogens. Epidemiologists, scientists, and developers, as well as regulators and funders, must collaborate to ensure that all cross-cutting operations are integrated properly in light of the continual threat of new diseases. In the realm of global health, much has been learnt about creating and administering vaccines in a way that ensures their equitable distribution and accessibility.

ETHICAL APPROVAL

This study was approved and got certificate from institutional research ethics committee faculty of pharmacy, university of Sargodha, Punjab Pakistan. Number of ethics committee approval: (20-IEC-32 UOS).

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