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Review Article

Vaccination in COVID-19

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Abstract: The study was done to determine the prevalence of Variant Creutzfeldt-Jakob disease prion among blood donors in Owo. The blood samples were collected from blood donorscertifed fit on account of negativity for HIV, HBsAg and HCV; at Federal Medical Centre Owo. Sera of participants were analysed using PRNP ELISA kit. Structured questionnaire was used to obtain demographic characteristic and other relevant information for the study. Out of the ninety blood donors screened for variant Creutzfeldt –Jakob disease prion none was found to be seropositive giving overall prevalence rate of 0%. Including screening for variant Creutzfeldt –Jakob disease in the blood safety policy of Nigeria is not advised, as of now. Surveillance should be sustained to review the policy, as the world is a global village.

Keywords: Covid-19, Vaccine hesitancy, Trust in science, Vaccine effectiveness, Trust in vaccine.

INTRODUCTION

In December 2019, the novel coronavirus (CoV) SARS-CoV-2 emerged in Wuhan, China and soon spread worldwide. This virus causes the condition referred to as "coronavirus disease 2019 (COVID-19).Coronaviruses are enveloped, positive-sense single-stranded RNA viruses ((+) ssRNA virus) belonging to the family *Coronaviridae [1-4]*. Many coronaviruses are known to infect humans. For example, 15–30% of common colds are caused by human coronaviruses (HCoVs) [5]. However; many coronaviruses are also zoonotic, which means that they primarily infect various animals. These zoonotic coronaviruses may be transmitted from animal reservoirs, such as bats, through an intermediate host (e.g., civet cats, camels, pangolins) to humans causing outbreaks, as seen during the severe acute respiratory syndrome (SARS) outbreak in 2002, the Middle East respiratory syndrome (MERS) outbreak in 2012, and now during the current COVID-19 pandemic [6-10]. When these zoonotic viruses infect humans, particularly those in older age groups with comorbidities or in patients with relevant risk factors (e.g., hypertension, allergic diseases, asthma, COPD), they can cause severe respiratory illnesses, such as acute respiratory distress syndrome (ARDS) and pneumonia, leading to death [11–14].

Since the onset of the COVID-19 pandemic, numerous tactics, such as increased emphasis on hand hygiene, social distancing, the donning of face coverings and gloves by the general public, and government stay-at-home orders have been used to reduce the spread of COVID-19 [6]. In spite of these efforts, SARS-CoV-2 has continued to spread, and as of July 14, 2020, it has resulted in over 13 million confirmed cases of COVID-19 and more than 570,000 deaths worldwide [9]. In addition to this toll on human life, this disease has disrupted workplaces, schools, and economies and strained healthcare systems with severe consequences. The total number of cases and fatalities from this deadly plague continues to climb daily, and some models suggest a potential resurgence of SARS-CoV-2 during the winter. These models also warn that without appropriate measures, such as intermittent social distancing, widespread surveillance, new therapeutics, and vaccines, critical care capacity may again be exceeded, and healthcare systems overwhelmed [19, 20]. As there is no specific therapeutics or vaccines in place to control COVID-19, attention has shifted toward preventing this

disease and other potential future resurgences of the virus through the research and development of a COVID-19 vaccine [21]. Currently, through the Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV) public-private partnership, numerous government agencies, including the National Institutes of Health (NIH), the Food and Drug Administration (FDA), and the Centers for Disease Control and Prevention (CDC), have partnered with representatives from academia, philanthropic organizations, and more than 15 biopharmaceutical companies to develop a safe and effective COVID-19 vaccine [9]. WHY VACCINE REQUIREMENT?

Despite significant reductions in disease morbidity and mortality credited to vaccines, some members of the public continue to remain skeptical as to whether vaccines, including a potential COVID-19 vaccine, are actually needed. Although the arguments surrounding this topic are multifaceted, perhaps the simplest approach is to determine if vaccines work and if they are superior to the existing alternatives (e.g., immunity derived from natural infection) [1]. Vaccine effectiveness refers to "the protection conferred by immunization in a defined population. It measures both direct (vaccine-induced) and indirect (population-related) protection," e.g., herd immunity. Vaccine effectiveness is directly related to the efficacy of the vaccine, but other factors, such as vaccine coverage, may also influence effectiveness [7]. The *direct effect* of vaccination is "the reduction in the probability of developing the disease, which is determined by comparing vaccinated and unvaccinated persons belonging to the same population [4, 5]." An example of the direct effect can be observed through the administration of the Hepatitis B vaccine to babies born to mothers who were positive for the Hepatitis B virus (HBV). Babies born to a mother with HBV have a 70–90% risk of developing chronic HBV infection; approximately 25% of these children may develop severe liver disease later in life [6, 8]. However, a longitudinal study was performed in which children born to mothers at high risk for HBV transmission were vaccinated with the HBV vaccine at birth and at 1, 2, and 12 months post-birth. Blood samples collected yearly for 20 years demonstrated that none of the study subjects acquired chronic HBV infections or clinical Hepatitis B disease, indicating a significant reduction in disease risk [9]. Similar reductions in incidence of disease have been observed in studies involving the Hepatitis A and *Haemophilus influenzae* (Hib) vaccines. This effective reduction in risk and incidence of disease must be determined with COVID-19 vaccination [3-5]. The *indirect effect* measures risk reduction for an individual who did not receive the vaccine [5, 1]. When most of a population is immune to an infectious disease, there is reduced transmission of the infection, which in turn protects individuals who are still susceptible [4, 5]. This concept is called "herd immunity." The basic reproduction number (R0) is defined as the average number of other individuals that each infected individual will infect. In general, the higher the R0 value, the greater proportion of the population that will need to be immune, either through natural infection or immunization, to reach the protective herd immunity threshold [4]. For example, the R0 for whooping cough, a disease caused by the bacterium *Bordetella pertussis*, is 5.5, meaning that one individual infected with whooping cough would likely infect 5–6 other people [5]. However, if 92–94% of the population is vaccinated against whooping cough, then the herd immunity threshold is reached, and the infected individual is significantly less likely to infect anyone else. This ultimately means that the spread of the disease is, in theory, blocked Vaccine necessity is dependent on whether vaccines work in reducing disease burden, and if they are superior to the alternative of natural immunization. Immunity can occur when a susceptible individual is exposed to a pathogenic agent and has a protective immune response. This exposure can occur in one of two ways, either naturally (from having the disease itself), as is the case when a person is exposed to influenza, or through medical interventions, which occurs when a person receives a vaccine. Some vaccine-hesitant individuals may object to vaccines on the grounds that natural immunization is better than immunization through vaccines. However, it is essential to recognize that although immunity can be obtained through either natural immunization or through vaccination, only vaccination allows the recipient to avoid exposure to diseases in a form that could cause disability or death [6]. COVID-19 symptoms can be unpredictable, with more mild forms causing fever/chills, cough, and fatigue and more severe forms leading to acute respiratory distress syndrome (ARDS), pneumonia, and death [2]. Similar to COVID-19, many vaccine-preventable diseases can either cause mild symptoms or severe complications depending on the individual infected. Therefore, a major benefit of vaccination is not just the buildup of immunity but also the reduction in severe manifestations of Safety of vaccine Disease [5].

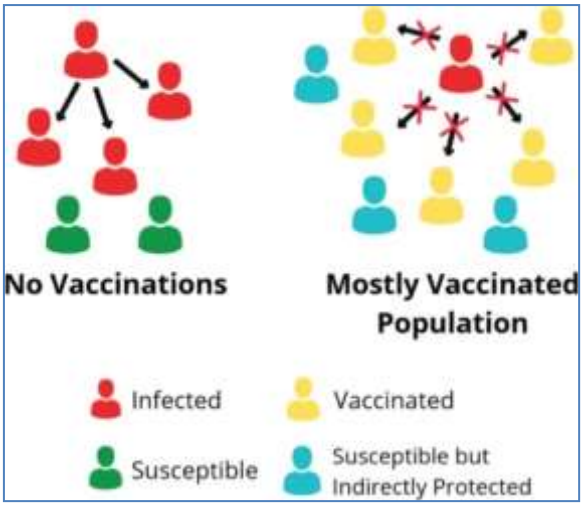

Fig-1: Possible results of vaccination

The first step in the potential production of a vaccine is determining whether or not the targeted disease-causing pathogen warrants a vaccine and if a suitable immunogenic target exists. Feasibility can be determined by various factors, such as number of strains of the target pathogen. This is part of the reason a vaccine against rhinoviruses, which have over 200 known strains, has not yet been developed. In addition, a pathogen, such as the rhinovirus, causes annoying yet usually non-life threatening infections. Thus, a good vaccine candidate would be one that causes significant disease with a limited number of strains or conserved immunogenic regions [4]. After it has been determined that a vaccine is warranted and feasible, vaccine development undergoes several stages of nonclinical and clinical testing followed by post-marketing surveillance. These phases are summarized in Table 1.

Table-1

Phase	Participants	Purposes
Nonclinical Phase	Computer modeling Cell line infectivity assays Animals receive test vaccine [7, 6]	Gauge vaccine safety and efficacy before administration to human subjects.
Investigational New Drug (IND) Application sent to FDA		
Phase I of Clinical Trials	20–100 healthy human volunteers receive test vaccine.	Assess whether the vaccine elicits an immune response in humans. Determine optimal vaccine dosage and route of administration. Gauge vaccine safety in humans [2,7]
Phase II of Clinical Trials	Several hundred human volunteers, many of whom will have characteristics similar to the target population for that particular vaccine, receive either the test vaccine or a placebo vaccine [3, 9].	Minimize confounding variables by administering either the test vaccine or a placebo-control vaccine to test subjects. Identify side effects in population of interest. Human subjects are often exposed to the pathogen under controlled conditions to test vaccine efficacy [7]
Phase III of Clinical Trials	Hundreds to thousands of at-risk human volunteers receive either the test vaccine or a placebo vaccine.	Detect uncommon side effects. Test vaccine efficacy under natural conditions by monitoring volunteers in their natural environments after receiving the test vaccine [7].
Vaccine licensed for administration to the public by the FDA.		
Phase IV (Post-marketing Surveillance)	The CDC and FDA investigate any suspected correlations between vaccines and unknown side effects that emerge after licensure. These suspected correlations can be reported by the general public via the Vaccine Adverse Events Reporting System (VAERS) or by health organizations through the Vaccine Safety Datalink (VSD).	Allows for detection of extremely rare side effects. Ensures continued safety even after licensure [7, 9]

As an additional note to the information provided in Table 1, vaccines are held to a higher standard of safety than many other medical products [8]. However, as with all medical products, no vaccine is perfectly safe or entirely effective. Vaccines can cause minor adverse events (AE), such as fever or local reactions at the injection site, or, on rare occasion, they can cause serious AEs, such as anaphylaxis [8]. Of the 317 million doses of vaccine distributed in the U.S. each year, the Vaccine Adverse

Events Reporting System (VAERS) receives approximately 40,588 reports of AEs following immunization. Each of these reports is accepted and entered without case-by-case determination of whether the AEs could have been caused by the vaccine in question (e.g., AEs that occur coincidentally after vaccine administration). Of the U.S. primary reports received between 2012 and 2016, 94.6% reported non-serious AE, 5% reported a serious nonfatal AE, and 0.4% reported death as the outcome. The first step in the potential production of a vaccine is determining whether or not the targeted disease-causing pathogen warrants a vaccine and if a suitable immunogenic target exists. Feasibility can be determined by various factors, such as number of strains of the target pathogen. This is part of the reason a vaccine against rhinoviruses, which have over 200 known strains, has not yet been developed. In addition, a pathogen, such as the rhinovirus, causes annoying yet usually non-life threatening infections. Thus, a good vaccine candidate would be one that causes significant disease with a limited number of strains or conserved immunogenic regions [2]. After it has been determined that a vaccine is warranted and feasible, vaccine development undergoes several stages of nonclinical and clinical testing followed by post-marketing surveillance. These phases are summarized in Table-2.

Table-2

Phase	Participants	Purposes
Nonclinical Phase	Computer modeling Cell line infectivity assays Animals receive test vaccine [7].	Gauge vaccine safety and efficacy before administration to human subjects.
Investigational New Drug (IND) Application sent to FDA		
Phase I of Clinical Trials	20–100 healthy human volunteers receive test vaccine.	Assess whether the vaccine elicits an immune response in humans. Determine optimal vaccine dosage and route of administration. Gauge vaccine safety in humans [2, 7]
Phase II of Clinical Trials	Several hundred human volunteers, many of whom will have characteristics similar to the target population for that particular vaccine, receive either the test vaccine or a placebo vaccine [9]	Minimize confounding variables by administering either the test vaccine or a placebo-control vaccine to test subjects. Identify side effects in population of interest. Human subjects are often exposed to the pathogen under controlled conditions to test vaccine efficacy [7]
Phase III of Clinical Trials	Hundreds to thousands of at-risk human volunteers receive either the test vaccine or a placebo vaccine.	Detect uncommon side effects. Test vaccine efficacy under natural conditions by monitoring volunteers in their natural environments after receiving the test vaccine [7]
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Misinterpretation & misinformation

The increased patient involvement can lead to improved health outcomes, as patients are more likely to follow treatment regimens that they are a partner in creating. However, potential setbacks can occur when patients acquire nonfactual information and choose the misinformation over the advice of their provider. This does not mean individuals should believe everything their doctor says without question, but rather that people should be hesitant to believe everything they read, especially concerning vaccines, on the Internet. This is

especially applicable to COVID-19 information, which often has little validation. This has caused many to become wary of treatments or vaccines, largely due to a falsified association between the MMR vaccine and autism [7, 8]. Misinformation regarding vaccines continues to spread throughout developed nations via the Internet, particularly through blogs and social media platforms [8]. With the current COVID-19 pandemic, numerous organizations are working round-the-clock to develop a vaccine, and some state governors are threatening the continuation of lockdowns until a vaccine is made available. In general, there is a growing distrust of the government and the healthcare system, in part due to subpopulations that have experienced historical and contemporary mistreatment and disparities in care [4]. Recent reports have demonstrated that long-standing health and social inequalities have put some minority groups, such as American Indian, African American, and Hispanic or Latino populations, at increased risk of COVID-19 infection or severe illness [9]. One option to rebuild public trust and promote health equity is for public health officials and medical professionals to work with community leaders outside of traditional medicine to develop and spread educational content regarding vaccines that is both readily accessible and culturally relevant [2]. Public health officials should work with respected community leaders, school nurses, disease survivors, and parents, as studies have demonstrated higher levels of trust in these groups among minority populations [9]. Working together, healthcare professionals and community leaders can educate and encourage the public to take an active role in using a potential COVID-19 vaccine to safeguard their individual health and the health of the community [9] For a society to function smoothly, citizens must exhibit cooperation and a certain degree of respect for one another. There are many occasions during which individuals will take actions that have a greater benefit for the community than for themselves. These altruistic actions often lead to the success of communities. In times of danger those who are able are called upon to defend those who cannot protect themselves. There are people who, through no fault of their own, are unable to receive vaccinations due to biological factors or health conditions. When people choose to get vaccinated, they are not only protecting themselves but also indirectly protecting those who cannot be vaccinated through herd immunity. The recent measles outbreaks are a reminder that if an increasing proportion of the population does not get vaccinated, then the disease can make a comeback.[5] It may encourage some people to know that by getting vaccinated, they are not only protecting themselves, but they are also protecting other vulnerable populations and contributing to eradicating certain preventable diseases [10].

LIMITATIONS

The limitations of this review arose from the nature of the virus described, which is unique. Vaccine development for the novel coronavirus is an ongoing process involving a large network of government, charitable, and biopharmaceutical organizations. This results in a constant stream of new information regarding the COVID-19 vaccine being published and updated. Therefore, as it currently stands, the exact type, mechanisms of action, and projected availability of the vaccine is yet to be determined. In addition, since vaccine hesitancy lies along a spectrum and misinformation can be promoted through a variety of sources, it is difficult to determine what the specific nature of the concerns and oppositions to the vaccine will be.

CONCLUSION

Since their development, vaccines have proven to be effective tools for the prevention of numerous deadly diseases [1]. Currently, there is no readily available vaccine for the novel coronavirus SARS-CoV-2, and the disease it causes, COVID-19. To prevent the continued spread of COVID-19, the ACTIV public-private partnership is working to safely develop and eventually administer the COVID-19 vaccine [2]. A major obstacle to vaccine administration is vaccine hesitancy, which is often due to concerns with the necessity or safety of vaccines, although many other concerns also exist [2, 7]. Based upon the principles of direct, indirect, overall effect and health economics there is a definitive need for the use of vaccines [4, 5]. When the need for a particular vaccine has been established, a rigorous series of trials and regulations have been created to ensure safety and efficacy. Even after licensure, the monitoring of approved vaccines continues, and all adverse events can be reported and tracked [7, 8]. Vaccine hesitancy lies along a spectrum and can vary greatly between individuals and communities. Therefore, public health officials and healthcare providers should work closely with community leaders to correct misinformation and promote the benefits of life-saving vaccines. If healthcare workers can collaborate effectively with members of their respective communities to create population-specific strategies to overcome vaccine hesitancy, many lives may be saved, and future shutdowns avoided [9, 10].

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