Official Publication of Pakistan Society of Biomass and Bioenergy
Journal of Biomaterials and Bio Products Technology
ISSN: 2790-2595 (Print), 2790-2609 (Online)
http://www.jbbt.org

SIGNIFICANCE OF VACCINES IN THE DETERRENCE OF DISEASES; AN UPDATE

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ABSTRACT

Vaccination is a biological preparation that gives active acquired immunity against a specific infectious disease. Vaccines are produced from attenuated form of microbes, its toxins and surface protein of microorganisms which causes disease. There are four types of vaccines (a) live attenuated vaccines (b) inactive vaccines (c) subunit recombinant polysaccharide and conjugated vaccines as well as (d) toxoid vaccines. Therefore, vaccines can be in the form of adjuvant, valence, excipients, and preservatives. There are many types of viral vaccines for different disease such as measles, mumps, rubella, vaccinia, varicella, zoster etc. The current example of viral disease is COVID 19 epidemic, which is causing serious health conditions in human population throughout the world. There have been 222,788,994 confirmed cases of COVID, with 4,600327 deathsand recorded cases were 199,314,577 as reported by WHO on September 8, 2021. To deal with this problem, experts of viral diseases from all over the world, particularly in wealthy countries, are frantically trying to create vaccines that could have the ability to treat coronavirus sufferers. However, a large portion of the world's population continues to wait for their fantasy medications to arrive in the markets. This review is aimed to explore the importance of vaccines for the immunization against various infectious diseases including the most promising anti-COVID-19 vaccine clinical trials as well as the mechanism of vaccine development and vaccination process in a biological system.

Keywords; Vaccine, COVID-19, Immunization, T-lymphocytes, DNA vaccines, RNA genome

Received: 13-04-2023, Revised: 15-05-2023, Accepted: 07-05-2023
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INTRODUCTION

The health of a country's population has an impact on its economic progress. Capital, health, and education are among the most important variables in a country's

development. Investments in the domains of health and education would hasten economic development (Ahmad,2021). Individuals' contributions to production and growth will increase if they are healthy. Every year many people get infectious diseases round the world so they may need vaccination to prevent these ailments before reaching to an incurable state. The vaccines train immune system to recognize and clear out the virus. The immune system of human body builds this protection after getting proper vaccination. Vaccine development and manufacture are both expensive and vulnerable to market failure. Many of the infectious diseases for which a vaccine is needed, such as HIV, malaria, and TB, are mostly found in developing nations. Because there is minimal financial potential, pharmaceutical and biotechnologycompanies have little motivation to produce vaccines for these illnesses. Financial rewards are generally limited, and financial and other risks are high, even in more prosperous countries. Too far, most vaccine development has relied on "push" financing from the government, universities, and non- profits. Many vaccinations have shown to be both cost-effective and helpful to the public health. Vaccine research and development is done out by a series of smaller organizations (Ahmad, 2021).

Mechanism of vaccine development

VLPs (viral like particles) are highly organized, repeating structures with a high density of viral capsid proteins. This high concentration of capsid proteins results in many conformational viral epitopes, which can trigger powerful immune responses. In the absence of any infectious nucleic acids from the virus, VLPs are generated by the self-assembly of viral capsid proteins (Figure 1). As a result of their complete inability to reproduce, they may be a safer alternative to the attenuated viruses typically used for vaccination (Dongarwar and Hamisu, 2021). Even in the absence of an adjuvant, VLPs have been demonstrated to trigger powerful immune responses. Structural proteins in the virion are often organized in a tight and well-ordered shape, which is thought to be recognized as a PAMP. As a result, delivering viral antigens in multimeric shape and as virus-like particles is one method to improve their immunogenicity (VLPs). VLPs made from enveloped and non-enveloped viruses can be utilized to immunize against the same virus or modified to includeepitopes from a different pathogen. VLPs are considered very safe

since they contain no genetic material, in addition to having greater immunogenicity. For decades, recombinant viruses have been employed as vectors for protein expression and immunization. The number of viral families being investigated as vaccine vectorsis far too long to be detailed, and the subject has lately been discussed elsewhere. Viruses may be modified to improve their safety and immunogenicity by removing virulence factors, altering tropism by switching envelope proteins, and boosting coding capacity by removing non-essential genes. The antigen is produced in the context of a real viral infection, which triggers innate immune responses necessary for the full

Recombinant proteins and synthetic peptides Delivering a viral antigen made by recombinant techniques or chemical synthesis is a safe way to trigger immune responses. Recombinant protein vaccines can have other benefits in addition to safety: First, manufacturing does not need pathogen manipulation, which eliminates the possibility of inadvertent escape as well as the challenges of bio-safety and bio-containment. Second, even with minimal information about the disease, vaccine candidates can be developed. Third, subunit vaccinations can be utilized to circumvent the

development of adaptive humoral and T cell-mediated immunity (Koirala *et al*., 2020).Competition of immune-dominant antigens from the vector or loss of effectiveness in the face of pre-existing immunity against the vector are potential drawbacks. The non- structural protein NSs is a key virulence factor that regulates the immunological response of the host, although it is not necessary for cell culture replication. Several organizations have produced viruses missing NSs through applying reverse genetics to attenuated strains and demonstrating safety and immunogenicity in mice and lambs.(Oyarzún and Kobe, 2016)

immune system's inherent preference for highly variable epitopes and steer immune responses toward conserved and widely protective epitopes. Fourth, because specificantigens elicit responses distinct from those elicited by natural infection, these vaccine techniques could be employed as DIVA (Differentiating Infected from Vaccinated Animals) vaccines with a serologicaltest(Leroux-Roels*et al*., 2011).The main disadvantage of subunit vaccines is that isolated proteins or peptides are usually poor immunogens because they

do not recognize Pathogen-Associated Molecular Patterns (PAMPs) and thus do not activate innate immune responses, which are necessary for the full development of acquired immunity. To boost immune responses to conserved epitopes, they must be delivered in an immunogenic form and/or be accompanied with a powerful agonist.(Wallis *et al*., 2019)

Nucleic acid vaccines

DNA vaccines provide a number of potential benefits for vaccinations against new viruses: plasmids expressing a viral antigen can be made quickly, even if only a partial sequence of the pathogen is known. Antigen generates both humoral and cell-mediated immune responses when it is produced in vivo. DNA preparations are more stable than other forms of vaccines and can be made in large quantities in a short amount of time at a lower cost, both of which are important qualities for a vaccine that must be utilized in distant places. Furthermore, DNA vaccines are regarded to be extremely safe, are ideal for DIVA applications, and are immune to anti-vector immunity (Maiyegun*et al*., 2021). The inherent poor immunogenicity of DNA vaccines is the primary impediment to their development. In prime-boost techniques, DNA vaccines are widely employed in conjunction with other vaccination platforms. Replicon vaccines are made up of faulty RNA genomes that can replicate and express encoded proteins but not form infectious virus particles. These plasmids can be utilized to encode a viral antigen, which can result in antigen-specific humoral and cellular immune responses. These findings sparked a massive amount of research into DNA-based vaccines for a variety of diseases, including influenza, HIV, and lymphocytic choriomeningitis virus (LCMV).DNA vaccines are more cost-effective than protein, whole cell, or viral vectors in practice because DNA can be generated using simple scalable chemistry or produced in large quantities in bacteria. Due to the limitations of DNA vectors, RNA-based vaccinations have gained popularity in recent years. They are low-cost and can be mass-produced quickly, similar to DNA-based vaccinations.(Oyarzun and Kobe, 2016; Leitner,2020)

However, the instability of RNA and ineffective in vivo distribution have traditionally limited its utility. To improve the intracellular stability of RNA molecules, several structural modification approaches have been used. Because RNA, unlike DNA, does not require targeting to and entry into

the nucleus, the fundamental obstacle that RNA vaccines must overcome is cell entry. This can be addressed by including polycationic carrier molecules in the formulation, which can condense and preserve the RNA while also facilitating its rapid cellular uptake (May, 2005).

Conjugate vaccines

Vaccines containing live, attenuated, or inactivated pathogens contain a variety of antigens, both polysaccharide and protein based. However, it is possible that only a limited number of them are needed to elicit protective immunity. The understanding that each protein has hundreds of potential immunogenic epitopes, not all of which are required has extended this reasoning to proteins (May,2005). Peptide-based vaccines have sparked interest because of this. Antigenic epitopes on a protein, on the other hand, are more than just a sequence of amino acids since the peptides utilized must imitate the immunogenic epitope's shape in the native protein. Computational modeling has proven to be a useful tool for locating and mapping the conformation of immunogenic epitopes within proteins. Because peptide or polysaccharide-based vaccines are less immunogenic than those found on a pathogen's surface, they require the addition of an adjuvant when administered (Sing *et al*.,2021). Another option is to conjugate the antigen to a second ‘helper' protein or polysaccharide that has been shown to boost immunogenicity; however, this may causethe immune response to be diverted toward the helper molecule. Approaches to circumvent this difficulty include careful matching and orientation of the target and helper sections of the vaccine, or spatial segregation of the two subunits using carrier systems like as liposomes (Metz *et al*., 2009).

Cellular vaccines

Attempts to employ a similar strategy to vaccinate against cancer have been made due to the history of success of immunization using live attenuated viruses, inactivated viruses, or bacteria. To generate an immune response against specific types of malignancies, attenuated tumor cells have been given. There have been two types of whole cell vaccines used: autologous and allogeneic. Cancers such as lung, colorectal, melanoma, kidney, and prostate cancer have all been studied with autologous cell vaccines. Autologous cell vaccines, on the other hand, are confined to a few types and stages of cancer since they require a significant amount of the patient's tumors for

preparation (Sorochi*et al*., 2021). Many whole cell vaccines have been genetically engineered to induce the expression of cytokines, chemokine's, and co-stimulatory molecules in order to boost immune activation. Another typeof cellular vaccination makes use of the patient's own immune cells, specifically dendritic cells. Dendritic cell vaccines are made by loading tumor-associated antigens or nuclei into a patient's autologous dendritic cells while they are being treated with immuno-adjuvants. In clinical studies, dendritic cell vaccines have been tested against prostate, melanoma, kidney, and glioma tumors. This vaccine regimen necessitates the collection of the patient's peripheral blood mononuclear cells, followed by cell culture processing and reinfusion, both of which are time-consuming and costly procedures. While these cell-based techniques are intriguing, they do not appear to contribute to the transition away from live and attenuated vaccines and toward vaccines with lower complexity and production costs that are better suited to treating large populations while decreasing health-care expenditures.(Oyarzún and Kobe, 2016)

Recombinant bacteria as vaccine vectors

Bacteria can be employed as vectors for the in vivo delivery of antigens or DNA, in addition to being widely used to manufacture recombinant subunit vaccines. The low cost and ease of scaling-up production, the availability of well-characterized attenuated strains, the vector's activation of innate immunity, and the efficient delivery to antigen-presenting cells are all potential advantages of this platform. Listeria, Salmonella, Lactococcus, and Bordetella are among the genera being investigated as vaccine vectors. Recombinant bacteria can be utilized as live vaccines, inactivated germs, or even bacterial ghosts with no cytoplasm. In mice, recombinant *Lactococcuslactis* expressing the SARS-coronavirus N protein has been demonstrated to produce antibodies(Wallis *et al*., 2019).

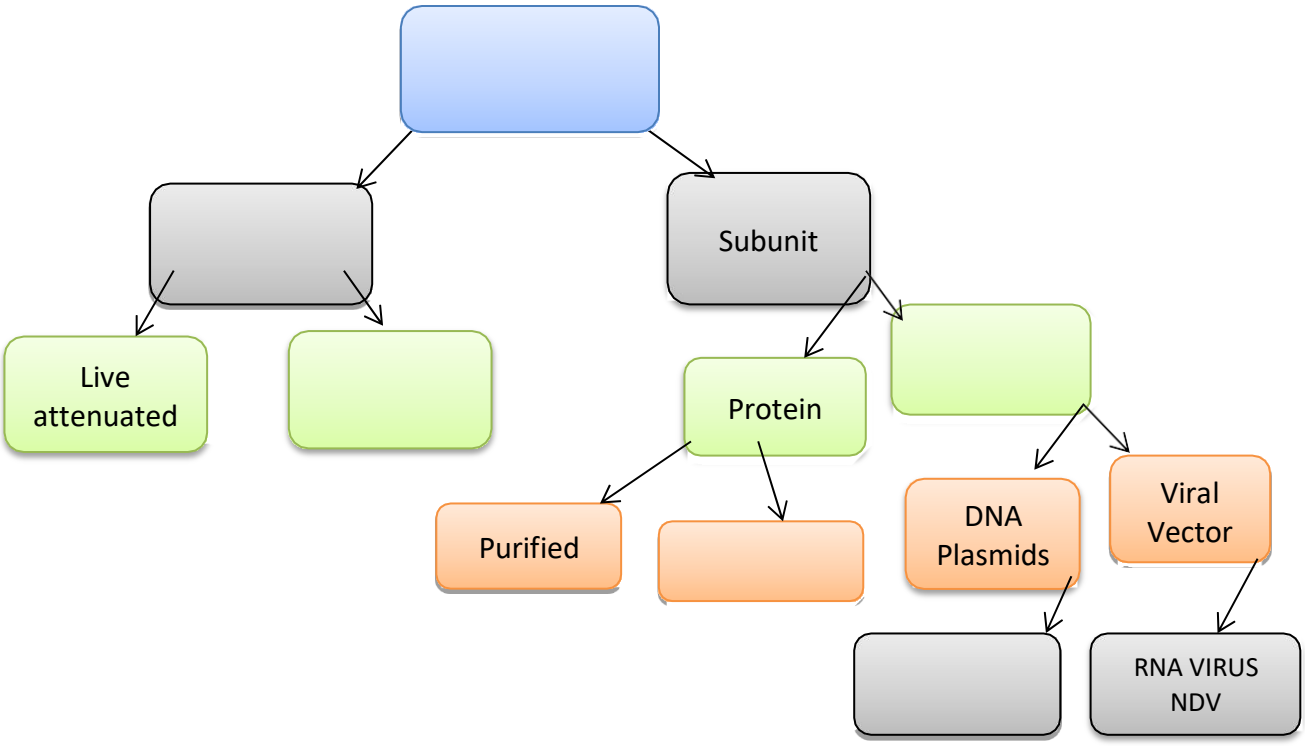

Figure1. Different steps forvaccine development

Immune Response to SARS-CoV-2 Virus

The immune system affects the severity of the COVID-19 disease. SARS-CoV-2 infection has an impact on both innate and adaptive immune responses. It has been described that SARS-CoV-2 enters the human body through physical barriers, such as respiratory tract, oral mucosa, and conjunctival epithelium. The dendritic cells, macrophages, and neutrophils represent the first line of defense, and their functions may be promoted by the production of type I and III interferons by SARS-CoV-2-infected epithelial cells. The adaptive T-cell- and B-cell-mediated immune responses are also presented in COVID-19 disease and, however, can be suppressed by SARS-CoV-2. In some cases, the innate immune cells may contribute to the excessive inflammation and, therefore, to the disease progression.The inability to reach control over the infection may result in dysregulated inflammatory responses that are potentially lethal. The IgM and IgG antibodies to SARS- CoV-2 are detectable within 1–2 weeks and began to decrease by 8 weeks. Several studies also reported that IgA response peaks earlierthan IgM. The antibody response particularlyleads to production of neutralizing antibodiesto the S protein and to the nucleoprotein. S protein is also the main target of the majority

of newly designed vaccines. The magnitude of neutralizing antibodies positively cell responses were detectable in individuals recovering from mild COVID-19 who did not have detectable antibody responses to SARS-CoV-2. The effective vaccination may not eradicate the SARS-CoV-2 virus but may at least protect from severe and deadly forms of the COVID-19 disease. Current knowledge regarding the diverse aspects of SARS-CoV-2-immune system interplay shall be reflected in the vaccine design, including the selection of antigens, the vaccine platforms and adjuvants, the vaccination routes, and the dosage regimen. The key points of the SARS-CoV-2 vaccination strategies are discussed below. To date, over 80 clinical trials have been registered in the Clinical Trials database by the National Library of Medicine at the US National Institutes of Health; however, only 34 of them are active and recruiting (11 of phase I, 8 of phase I/II, 3 of phase II, 1 of phase II/III, and 11 of phase III). Moreover, 2 vaccine candidates have been approved for use by the US *Food and Drug Administration* (FDA) – BNT162/Comirnaty and mRNA-1273). BNT162/Comirnaty has been also permitted by the *European Medicines Agency* (EMA). The vaccination program with BNT162/Comirnaty has been recently initiated in many European countries.

Inactivated Vaccines

Inactivated vaccines are based on presenting the form of pathogen with a loss of disease-producing capacity. The virus cultivation occurs in cell lines that represent a substrate for the production of large quantities of antigen. Virus multiplication is often followed by a purification and concentration prior to the vaccine inactivation. Formaldehyde and beta-propiolactone are used in the majority of licensed human antiviral vaccines to inactivate the virus. Multiple doses or adjuvants are required to achieve sufficient efficacy of inactivated vaccines. To date, 4 inactivated vaccines have reached the phase III clinical trials and are currently under evaluation (#NCT04510207, #NCT04508075, and #NCT04456595).

DNA Vaccines

DNA vaccines deliver coronavirus's genes to the human cells. The vaccination principle depends on the DNA translocation into the cell nucleus where the transcription of the antigen is initiated and followed by a translation. DNA vaccines frequently use

plasmids as vectors. Depending on the route of vaccine administration (intramuscular, intradermal, and subcutaneous), either myocytes or keratinocytes are addressed. Nonetheless, antigen-presenting cells residing close to the site of application can be transfected directly by DNA vaccines as well. In such cases, the expressed antigens are loaded onto MHC I and MHC II molecules due to the cross-priming potential. The produced antigens are either released by exosomes or apoptotic bodies which lead to a recognition by antigen-presenting cells and further evolvement of humoral or cytotoxic immune responses. Different delivery devices are used to create a robust immune response. The main safety concerns imply a possible integration of transfected DNA into somatic and/or germ cells of the host. In such cases, a dysregulation of gene expression might occur and lead to various mutations. However, only extrachromosomal plasmids with a very low level of chromosomal integration are usually employed in the development of DNA vaccines. Furthermore, the majority of plasmids remain at the site of administration.

RNA Vaccines

Messenger RNA (mRNA) vaccines were first tested in early 1990s; however, their use was limited because of their instability. The mRNA encodes the genetic information to produce an antigen, and thus, RNA vaccines also lead to a production of coronavirus's proteins in vivo. The in vitro generation of an RNA vaccine includes a reaction of a DNA plasmid template and a recombinant RNA polymerase. In addition, a synthetic cap analog and a poly(A) tail are added to form a mature RNA sequence. The stabilization is further achieved by various transport systems (such as lipid nanoparticles, nano-emulsions, and cationic peptides) or methods enabling facilitated transfection (gene gun and electroporation). Conventional mRNA vaccines are based on the initiation of the transient antigen expression in the cytoplasm of the host cells. Another platform is represented by self-amplifying mRNA vaccines that contain both the genes coding the targeted antigen as well as the genes required for the self-replication (mostly RNA-dependent RNA polymerase). The conventional mRNA vaccines induce a prompt antigen expression, and the expressed antigens generate both humoral and cellular immune responses. In self-amplifying mRNA vaccines, a delayed antigen expression may prevail and limit the efficacy of the vaccine. Yet, the self-amplifying

mRNA vaccine platform reaches higher yields, and thus, an equivalent protection is abovementioned platforms are not capable of producing viral particles due to the lack of viral structural proteins. Moreover, neither conventional nor self-amplifying mRNA vaccines can integrate into the host genome. The mRNA-based vaccines were able to conferred at much lower doses. Regarding the safety profiles, the replicons of both induce production of functional antibodies with neutralizing properties in rabies, influenza, or Zika virus and also represent a promising vaccination strategy in the prevention against COVID-19 infection.

NOVEL VACCINE DESIGNS

Virus-like particles

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development of adaptive humoral and T cell-mediated immunity (Koirala *et al*., 2020).

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Veterinary Vaccine

Vaccination of animals is used to prevent disease in the animals as well as disease transfer to people. Animals maintained aspets and cattle are both immunized on a regular basis. Wild populations may be vaccinated in some cases. This is often achieved by disseminating vaccine-laced food in a disease-prone region, and it has been used to reduce rabies in raccoons. Rabies vaccination of dogs may be mandated by legislation in areas where rabies is present. Canine distemper, canine parvovirus, infectious canine hepatitis, adenovirus-2, leptospirosis, bordatella, canine Para influenza virus, and Lyme disease are among the various vaccinations available for dogs. Veterinary vaccinations have been administered in people, whether intentionally or accidentally, resulting in certainincidences of disease, most notably brucellosis. However, such occurrences are seldom reported, and little research has beendone on the safety and outcomes of suchtreatments. Human exposure to infections that are not naturally borne in humans, such as Bordetellabronchiseptica, has undoubtedly

risen since the introduction of aerosol immunization in veterinary clinics for veterinary vaccination against a disease can be orders of magnitude less expensive than the human vaccine (Bakarey,2021).

companion animals in recent years. In certain situations, like as rabies, the

Differentiation of Infected from Vaccinated Animals (DIVA) Vaccines

Differentiation of Infected from Vaccinated Animals (DIVA) vaccines, also known as SIVA (Segregation of Infected from Vaccinated Animals), allow infected and vaccinated animals to be distinguished. The microorganisms prevalent in the field carry at least one epitope less than DIVA vaccines. We can make that distinction with the use of a diagnostic test that detects antibodies against that epitope. Oirschot in 2003 worked in the Central Veterinary Institute in Lelystad (Netherlands) has produced the first DIVA vaccinations (previously known as marker vaccines, and since 1999 known as DIVA vaccines) and companion diagnostic tests. They discovered deletions in the viral genomes of certain current vaccines against pseudorabies (also known as Aujeszky's illness) (among which was the gE gene). DIVA vaccines and associated diagnostic tests for bovine herpesvirus 1 infections have been developed along the same lines (Koirala *et al.*, 2020). The DIVA method has effectively eliminated the pseudorabies virus in a number of nations. Swine populations were heavily vaccinated and monitored using a companion diagnostic test, and diseased pigs were then culled from the herd. Bovine herpesvirus 1 is a virus that infects cattle. In addition, DIVA vaccinations are frequently utilized in clinical practice. Scientists have worked hard to adapt the DIVA principle to a variety of infectious illnesses, including classical swine fever, avian influenza, Actinobacillus pleuropneumonia, and Salmonella infections in pigs, among others (Sing *et al.*,2021; Weniger *et al.*,1999;Wirsiy *et al.*,2021).

Clinical development

Clinical development is divided into three stages (Fig.2). Small groups of people are given the experimental vaccine during phase I. The clinical research is expanded in phase II, and the vaccine is given to persons who have characteristics (such as age and physical health) that are similar to those who will benefit from the new vaccine. Thousands of people are given the vaccine in phase III, and it is examined for efficacy and safety. After a

vaccine is approved and licensed, it is subjected to Phase IV formal, ongoing trials. The Phase I study involves introducing the vaccine candidate to healthy people in order to determine its safety. The Phase I study involves introducing the vaccine candidate to healthy people in order to determine its safety. A Phase I vaccination study consists of healthy volunteers who are given either the candidate vaccine or a "control" treatment, such as a placebo or an adjuvant-containing cocktail, or a proven vaccine (which might be intended to protect against a different pathogen). The major goal of the test is to look for signs of safety (no adverse events) and evidence of an immunological response.(Leroux-Roels *et al.*, 2011)

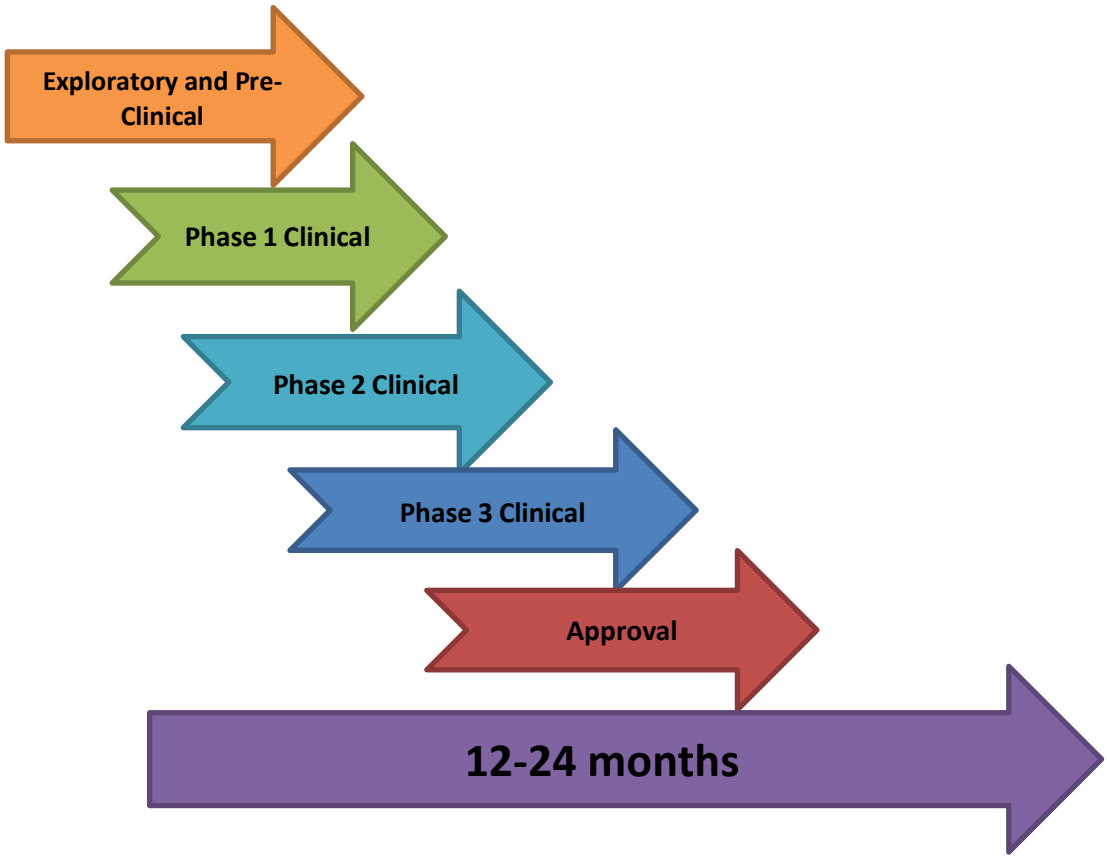

Figure 2. Different phases of vaccine development

Regulatory review and approval

Nearly every stage of vaccine development, manufacture, and marketing clearance involves regulatory difficulties. Regulations apply from the time a vaccine is designed and

clinically tested, through manufacture, and distribution to the general public (May, 2005).

Manufacturing

Vaccine production is a lengthy process. Vaccines take anything from 7 to 36 months to manufacture, package, and deliver to thosein need. It entails testing each batch of

Quality control

Vaccine quality control used to rely on a range of testing procedures to guarantee thatthe products were safe and effective. These techniques were created for vaccines whose safety and efficacy were determined after years of research. However, as vaccine manufacturing technology has advanced.Tests can now detect potential risks with a sensitivity that wasn't conceivable just a fewyears ago, and a growing number of physicochemical approaches allows for considerably improved product

CONCLUSION AND FUTURE PROSPECTS

Successful vaccine manufacturing necessitates international standardization of starting materials, production and quality control testing, and the establishment of high expectations for regulatory oversight of the entire manufacturing process from start to finish, all while acknowledging that this fieldis constantly changing. All components, production processes, testing methods,

vaccination at each stage of its trip, as well asrepeated quality monitoring of batches byvarious authorities throughout the world (Lerous-Roels*et al*.,2011)

characterization. Vaccine regulation includesa number of different measures in addition to sophisticated tests to verify safety. These include supplier audits for characterization ofstarting materials, cell banking, seed lot systems, adherence to GMP principles, independent release of vaccines on a lot-by- lot basis by national regulatory authorities, and enhanced pre- and post-marketing surveillance for possible adverse events after immunization.(Metz *et al*., 2009)

reagents, and standards must adhere to the GMP. Pharmaceutical quality systems, quality assurance techniques and processes, multiple quality controls at each level give guarantee vaccine identity, purity, sterility, efficacy and safety, and suitableinfrastructure are all part of these stringent quality criteria (Sorochi *et al*.,2021)

- The vaccine's efficacy or performance is determined by a number of factors, including the disease itself (for some diseases vaccination performs better than for others)
- The vaccination strain (some vaccines are specific to, or at least most effective against, particular strains of the disease)
- Whether the immunization schedule was followed correctly.
- A person's unique reaction to vaccination; some people are "non-responders" to specific vaccines, meaning they do not produce antibodies even after being properly vaccinated.
- Ethnicity, age, or genetic susceptibility, to name a few.

The following are important factors to consider when determining the efficacy of a vaccination programmer:

1. Carefulmodeling to predict the impact of an immunization campaign on disease epidemiology in the medium to long term
2. Ongoing surveillance for the relevant disease following the introduction of a new vaccine
3. Maintaining high immunization rates, even when a disease has become rare.

Vaccines for more than 20 life-threatening diseases are now available, allowing individuals of all ages to enjoy longer, healthier lives. Every year, vaccines prevent 2-4 million deaths from diseases such as diphtheria, tetanus, pertussis, influenza, and measles. Immunization is an indisputable human right and an important component of primary health care. It's also one of the most cost-effective health investments available. Vaccines are also important for preventing and controlling infectious disease outbreaks. They are essential in the fight against antimicrobial resistance and support global health security (Wirsiy *et al.*,2021). Despite significant advances, far too many people around the world – including approximately 20 million infants each year – lack adequate immunization access. Progress has slowed or even reversed in some nations, and there is a serious danger that complacency will destroy previous successes (Wallis *et al*.,2019)

Vaccines contain pure materials obtained from dead or inactivated organisms. Vaccines come in a variety of shapes and sizes. These are many approaches of reducing

the risk of sickness while maintaining the ability to elicit a positive immunological response. Vaccines can be monovalent (also known as univalent) or multivalent (also known as multivalent) (also called polyvalent). A monovalent vaccine is intended to protect against a single antigen or microbe. A multivalent or polyvalent vaccine protects against two or more strains of the same microbe, or two or more germs altogether. A Greek or Latin prefix might be used to indicate the valiancy of a multivalent vaccine (e.g., tetravalent or quadrivalent). A monovalent vaccine may be beneficial in some situations for eliciting a high immune response quickly. When two or more vaccines are combined in the same formulation, they will create problems (Sing *et al*.,2021) This is particularly common with live attenuated vaccinations, in which one of the vaccine components is stronger than the others, suppressing the growth and immune response to the others. This behavior was originally observed with the trivalent Sabin polio vaccine, where the amount of serotype 2 viruses in the vaccine had to be lowered to avoid interfering with the "take" of the serotype 1 and 3 viruses. This behavior has also been discovered to be a problem with current dengue vaccines in which the DEN-3 serotype predominates and suppresses the response to the DEN-1, 2, and 4 serotypes. When it's time for a booster, people who have had a bad reaction to adsorbed tetanus toxoid may be given the basic vaccine.(Yang *et al*., 2016)

Preservatives may be added to vaccines to avoid contamination by bacteria or fungi. Preservatives may be utilized at many phases of vaccine manufacture, and the most advanced measurement methods mayidentify residues of them in the completed product, just as they may in the environment.

The following excipients and leftover manufacturing chemicals are present or may be present in vaccine formulations, in addition to the active vaccine:

- Adjuvants such as aluminum salts or gels are used.
- Adjuvants are added to vaccines to stimulate a faster, more powerful, and longer-lasting immune response, allowing for a lower vaccinationdose.
- Antibiotics are used in certain vaccinations to prevent bacteria from growing during manufacturing and storage.

- Because influenza and yellow fever vaccinations are made from chicken eggs, they include egg protein. Other proteins might be present as well.
- Toxoid vaccinations utilize formaldehyde to inactivate bacterial products.
- In a few vaccines, stabilizers such as monosodium glutamate (MSG) and2-phenoxyethanol are used to keep the vaccine stable whether it isexposed to heat, light, acidity, or humidity.
- Thiomersal is a mercury-based antibacterial that is added to vaccination vials containing several doses to avoid contamination and the development of potentially dangerousmicroorganisms.

ACKNOWLEDGEMENT

Participation of all authors are highly appreciated and acknowledged.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest for publication of this review.

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