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Review Article

Vaccines: A Comprehensive Review of Vaccine Evolution and mRNA Technology

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ABSTRACT

Vaccines have saved millions of lives and reduced the spread of infectious diseases, thereby transforming global health. This comprehensive overview traces the historical evolution of vaccines-from ancient inoculation practices to Edward Jenner's smallpox vaccine and the groundbreaking development of modern mRNA vaccines. It categorizes vaccination forms, such as viral vector, subunit, toxoid, live attenuated, and inactivated vaccines, explaining their mechanisms and appropriate applications. The essay also explores the role of carriers and delivery systems such as Lipid Nanoparticles (LNPs), viral vectors, and protein conjugates that enhance vaccine efficacy and stability. Additionally, the importance of adjuvants like aluminum salts and newer emulsions in boosting immune responses is discussed. A special focus is given to mRNA technology, which emerged as a transformative platform during the COVID-19 pandemic. Unlike traditional vaccines, mRNA vaccines instruct host cells to produce antigens, offering rapid, scalable, and adaptable immunization strategies. Advantages of mRNA vaccines include their safety profile, modular production, and application potential beyond infectious diseases, notably in cancer immunotherapy and genetic disorder treatment. Despite their benefits, challenges such as cold-chain storage, limited durability of immune protection, and vaccine hesitancy remain. Ethical concerns related to rapid approvals and global inequity in vaccine distribution also require attention. As vaccine science advances, equitable access, robust regulatory oversight, and public trust will be a necessity that harness emerging technologies potential like mRNA. This essay underscores the central role of vaccines and innovative platforms in shaping the future of medicine and public health.

Keywords: mRNA Vaccines, Vaccine Types, Delivery Systems, Immunization History, Lipid Nanoparticles.

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INTRODUCTION

Biological preparations known as vaccines stimulate the body's immune system to identify and fight off invaders, resulting in active acquired immunity to particular infectious diseases. They typically contain agents that resemble a disease-causing microorganism-these may be weakened or inactivated forms of microbes, specific protein (subunits), or hereditary material such as mRNA-that cause the immune system to react without causing disease itself (Plotkin, 2014). In action, the immune system releases antibodies and memory cells which rapidly respond to further exposures, thereby preventing illness. Vaccines have been essential to public health, eliminating or drastically lowering the incidence of illnesses like measles, polio, and smallpox (Andre *et al.*, 2008). In addition to protecting individuals, widespread vaccination contributes to herd immunity, reducing disease transmission within communities. Overall, vaccines remain among the most effective and cost-efficient tools in disease prevention and global health advancement.

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Historical Background of Vaccines

The concept of immunization dates back over a thousand years, with early forms of inoculation practiced in China, India, and the Ottoman Empire (Plotkin, 2014). Edward Jenner's work in 1796 marked the beginning of the modern era of vaccination, when he demonstrated that inoculation with cowpox could protect against smallpox-a practice that came to be known as vaccination (Riedel, 2005). By creating rabies and anthrax vaccines later in the 19th century, Louis Pasteur furthered scientific advancements based on attenuated (weakened) pathogens.

The creation of vaccinations during the century 20 expanded rapidly. Landmark achievements included Jonas Salk's Inactivated Polio Vaccine (IPV) in 1955, while Albert Sabin developed the

Oral Polio Vaccine (OPV) in 1961. Vaccination programs led by WHO (World Health Organization) helped eradicate smallpox worldwide by 1980 and bring polio close to eradication in the majority of nations (WHO, 2020). Different vaccine and their characteristics are listed in Table 1.

Types of Vaccines

Based on their structure and the way elicit an immune response, vaccines can be broadly divided into several categories.

The primary categories include:

Vaccines with Live Attenuation

These vaccines employ a weakened version of the live pathogen, which is capable of replicating but does not infect healthy people. Vaccines against varicella (chickenpox), yellow fever, Measles, Mumps, and Rubella (MMR) are a few examples (CDC, 2022). They may not be appropriate for immunocompromised people, but they usually elicit robust and sustained immunological responses.

Killed or Inactivated Vaccines

Bacteria or viruses that have been destroyed by physical or chemical means are used in inactivated vaccinations. These vaccines are safer for those with compromised immune systems since they cannot reproduce. Inactivated Polio Vaccine (IPV) and hepatitis A vaccination are two examples (CDC, 2022).

Conjugate, polysaccharide, recombinant, and subunit vaccines

These vaccines work by using certain pathogen components, like proteins or carbohydrates, to elicit an immune response. The Human Papillomavirus (HPV) and hepatitis B vaccinations, for example, are subunit vaccines. Vaccines that connect polysaccharides to proteins, such those for Haemophilus influenzae type b (Hib), increase immunogenicity, particularly in newborns (Plotkin *et al.*, 2017).

Vaccines using Toxoids

Instead of using the actual bacteria, toxoid vaccinations use inactivated toxins that the bacteria create. The vaccinations for diphtheria and tetanus are two examples. Instead of attacking germs, these vaccines teach the immune system to fight off poisons (CDC, 2022).

The mRNA vaccines

Synthetic messenger RNA is used in mRNA vaccines, a revolutionary platform that directs cells to manufacture a viral antigen, like the spike protein seen in SARS-CoV-2. The protein causes an immunological reaction after it is created. Pfizer-BioNTech and Moderna's COVID-19 vaccines made use of this platform with success (Pardi *et al.*, 2018).

Vector-borne Vaccines

These vaccinations transfer genetic material from the target pathogen using a harmless virus as a vector. The genetic material tells the cells to make antigens once they are inside the host cells. Adenoviral vectors are used in the AstraZeneca COVID-19 vaccines, for instance (Folegatti *et al.*, 2020).

Basic Concepts of Immunology and Vaccines

The study of immunology focuses on the immune system, which uses an intricate network of cells, chemicals, and processes to defend the body against pathogens. One key components of this system is the antigen-a molecule, typically a protein or polysaccharide found on the surface of pathogens-which the immune system perceives as alien and sets forth an immunological reaction (Murphy and Weaver, 2016). The first reaction to infection is the innate immune response, which acts rapidly but without specificity, involving dendritic cells, macrophages & neutrophils. These cells eliminate microbe through phagocytosis & antimicrobial substances are released. Major Histocompatibility Complex (MHC) molecules are used by Antigen-Presenting Cells (APCs), particularly dendritic cells, to process antigens and show them on their surface (Chaplin, 2010).

By activating T lymphocytes and B cells, the adaptive response is more focused and offers sustained protection. While CD8+ cytotoxic T cells identify MHC class I-associated antigens and eliminate infected cells, CD4+ helper T cells identify antigens presented by MHC class II molecules and aid in coordinating the immune response. After being activated, B cells develop into plasma cells that generate antibodies, which are specialized proteins called immunoglobulins that attach to antigens, destroy infections, and mark them for elimination. The combined efforts of these immune cells are called effector functions, including cytokine release, inflammation, phagocytosis, and direct cell killing (Murphy and Weaver, 2016).

A crucial aspect of the adaptive immune system is immune memory, the capacity to react to viruses more successfully after first encountering them. This is accomplished by producing memory B and T cells, which endure following an infection or immunization. The first exposure to an antigen results in a primary immune response, which is slower and less robust. With repetitive exposure of similar antigen, the immune system generates a response more faster powerful response as memory cells recognizes it (Janeway *et al.*, 2001).

Vaccine Carriers and Delivery Network

Vaccine efficacy frequently hinges on the use of adjuvants and carriers to improve the vaccine's stability and immune response.

Lipid based Nanoparticles (LNPs)

LNPs, critical component in mRNA vaccine delivery. They enable entrance into cells and shield mRNA from deterioration. Use of

LNPs has enabled the successful deployment of mRNA vaccines by improving stability & uptake for prevention of COVID-19 (Hou *et al.*, 2021).

Viral Vectors

As mentioned, viral vectors serve as carriers for genetic material. Adenoviruses are commonly used due to their ability to infect human cells and induce robust immune responses. These carriers can be replication-deficient to enhance safety (Logunov *et al.*, 2020).

Protein Carriers in Conjugate Vaccines

Polysaccharides from bacterial cell walls are poorly immunogenic on their own, especially in young children. Conjugate vaccines use carrier proteins such as diphtheria or tetanus toxoids to improve immune recognition. This approach is used in vaccines against Hib, pneumococcal, and meningococcal diseases (Gossger *et al.*, 2009).

Microneedle Patches and Oral Vaccines

Innovative delivery method including oral formulation & microneedling patch are under investigation to improve accessibility and compliance. These approaches aim to eliminate the need for needles, reduce cold chain requirements, and simplify mass vaccination campaigns (Kim *et al.*, 2012).

Adjuvants in Vaccines

Adjuvants are chemicals that are included in vaccinations to improve body's immune system. Aluminum salts (alum) are a commonly used adjuvant, used for decades to improve antigen presentation (Awate *et al.*, 2013). Newer adjuvants like AS03 and MF59, used in some influenza vaccines, are oil-in-water emulsions that help recruit immune cells to the site of injection (Reed *et al.*, 2013).

mRNA Techniques and Vaccines: Revolutionizing Modern Medicine

Messenger RNA (mRNA) technology represents one of the most significant advancements in biomedical science in recent years. Although mRNA was discovered in the early 1960s, it is only recently-with the advent of mRNA-based COVID-19 vaccines-that this technique has demonstrated its transformative potential in clinical practice. mRNA vaccines offer a new approach to disease prevention and therapy, differing fundamentally from traditional vaccine platforms. This essay explores the principles behind mRNA technology, its application in vaccines, its advantages and challenges, and its broader implications in the treatment of various diseases.

Understanding mRNA Technology

A particular kind of RNA molecule called mRNA transports genetic instructions from DNA to the ribosomes, which are the cell's machinery enabling cells to produce specific proteins essential for various biological functions (Sahin *et al.*, 2014). Unlike DNA-based treatments, mRNA does not enter the nucleus or alter the genetic material of the host. Instead, synthetic mRNA can be designed to encode virtually any protein and introduced into human cells, which help the target protein to get immediately translated.

However, due to its intrinsic instability, mRNA degrades quickly. For decades, this instability posed a barrier to therapeutic applications. Researchers overcame these issues by modifying the mRNA's structure-for example, through nucleoside modifications-and by packaging mRNA within lipid-based nanoparticles which gives protection from enzyme to degrade & facilitate cellular uptake (Karikó *et al.*, 2005). These innovations cleared the path for mRNA based vaccines development.

mRNA Prophylactics & Virus COVID-19

The global outbreak of COVID-19 provided the first large-scale opportunity to deploy mRNA vaccines. Moderna's mRNA-1273 and Pfizer-BioNTech's BNT162b2 became the first mRNA vaccines authorized for use in emergency situations, demonstrating efficacy rates above 90% in trials (Polack *et al.*, 2020; Baden *et al.*, 2021). The spike (S) protein of SARSCoV-2 is encoded by these vaccinations. The spike protein, which is produced by cells upon injection, sets off an immunological reaction that includes T-cell activation and the production of neutralizing antibodies.

The speed of mRNA vaccine development was unprecedented. Once the genetic sequence of the virus was published, vaccine candidates were designed within weeks, and clinical trials began shortly after. This rapid response was made possible by the flexibility of mRNA platforms and pre-existing research infrastructure.

Advantages of mRNA Vaccines

mRNA vaccines have several advantages over conventional platforms. First, they are faster and easier to design. Because they do not require growing pathogens or proteins in the lab, vaccine production can be rapidly scaled in response to emerging threats (Pardi *et al.*, 2018). Second, mRNA vaccines are non-infectious and do not integrate into the genome, offering a favorable safety profile.

Manufacturing mRNA vaccines is also more modular and adaptable. Once an mRNA production facility is established, it can be used to produce vaccines for different diseases by simply changing the genetic sequence being encoded. Additionally, LNP delivery systems can be used across a range of mRNA-based formulations, enhancing consistency in development.

Obstacles and Restrictions

mRNA vaccines have significant obstacles in spite of their advantages. Their susceptibility to temperature is one of the main problems. Initially, the Pfizer-BioNTech vaccine needed to be stored at -70ºC, which made distribution more difficult, especially in in areas with low incomes (WHO, 2021). Though stability improvements have been made, cold-chain requirements remain a logistical hurdle.

Another limitation is the durability of immune responses. Protection may wane over time, necessitating booster shots, especially in the face of new viral variants (Bar-On *et al.*, 2021). To ascertain the durability of immunity and the possibility of uncommon side effects, long-term research is still being conducted.

Public skepticism and misinformation also pose obstacles. Vaccine hesitancy, fueled by misunderstanding or mistrust of novel technologies, has hindered uptake in some populations. Transparent communication about how mRNA vaccines work, their safety profiles, and their benefits is crucial for public trust.

Applications beyond Infectious Disease

New therapeutic options have become available as a result of the effectiveness of COVID-19 mRNA vaccines. mRNA technology is being tested for other infectious diseases such as influenza, Cytomegalovirus (CMV), and Zika. Moderna has several mRNA vaccines in development for these and other pathogens (Moderna, 2023).

Cancer is another promising area. Tumor-specific neoantigens are the focus of personalized mRNA cancer vaccines. These vaccines aim to enable the immune system to identify and eliminate cancer cells according to each patient's particular. Early-phase

Table 1: Vaccines and their characteristics.

Vaccine Name	Type	Carrier/Platform	Year Developed	Primary Use	Citation
Smallpox (Jenner)	Live (related virus – cowpox)	Natural cowpox virus	1796	Eradication of smallpox	Riedel, (2005)
BCG (Tuberculosis)	Live attenuated	Mycobacterium bovis	1921	Prevention of tuberculosis	WHO, (2020)
Inactivated Polio (IPV)	Inactivated (killed virus)	Formalin-inactivated poliovirus	1955	Prevention of poliomyelitis	Plotkin *et al.*, (2017)
Oral Polio (OPV)	Live attenuated	Attenuated poliovirus	1961	Mass immunization for polio	Plotkin *et al.*, (2017)
MMR	Live attenuated	Attenuated measles, mumps, rubella	1971	Prevention of measles, mumps, rubella	CDC, (2022)
Hepatitis B	Subunit recombinant	Recombinant surface antigen (HBsAg)	1986	Prevention of hepatitis B and liver cancer	WHO, (2020)
HPV (Gardasil)	Subunit recombinant	Virus-like particles (VLPs)	2006	Prevention of HPV-related cancers	CDC, (2022)
Pneumococcal (PCV13)	Conjugate	Polysaccharide + diphtheria protein	2010	Prevention of pneumococcal diseases	Plotkin *et al.*, (2017)
Hib	Conjugate	Polysaccharide + tetanus toxoid	1987	Prevention of Haemophilus influenzae type b	Gossger *et al.*, (2009)
Tetanus	Toxoid	Inactivated tetanus toxin	1924	Prevention of tetanus	Plotkin *et al.*, (2017)
COVID-19 (Pfizer-BioNTech)	mRNA	Lipid nanoparticles (LNPs)	2020	Preventing COVID-19	Polack *et al.*, (2020)
COVID-19 (Moderna)	mRNA	Lipid nanoparticles (LNPs)	2020	Preventing COVID-19	Baden *et al.*, (2021)
COVID-19 (AstraZeneca)	Viral vector	Chimpanzee adenovirus (ChAdOx1)	2020	Preventing COVID-19	Folegatti *et al.*, (2020)
Rabies (Human diploid cell)	Inactivated (killed virus)	Human diploid cells	1976	Post-exposure rabies prophylaxis	WHO, (2020)

trials have shown encouraging results in melanoma and other cancers (Sahin *et al*., 2017).

In addition, researchers are exploring mRNA therapies for genetic disorders. By delivering mRNA that encodes a functional version of a missing or defective protein, it may be possible to treat conditions like cystic fibrosis or certain enzyme deficiencies without altering the DNA.

Ethical and Regulatory Considerations

As with all biotechnologies, mRNA techniques raise ethical and regulatory concerns. Emergency authorizations during the COVID-19 pandemic involved compressed timelines and increased public scrutiny. While safety was rigorously evaluated, the speed of development highlighted the need for robust post-marketing surveillance systems.

Equity is another key issue. The unequal global distribution of mRNA vaccines revealed disparities in healthcare infrastructure and access. Moving forward, ensuring that mRNA-based treatments are equitably distributed will require international cooperation, investment in manufacturing capacity in low-income countries, and licensing frameworks that promote global access.

CONCLUSION

The evolution of vaccines is a testament to humanity's resilience and ingenuity in combating infectious diseases. From ancient inoculation practices to the revolutionary development of mRNA technology, vaccines have significantly reduced global disease burdens and saved countless lives. This comprehensive overview highlights how various vaccine types-inactivated, subunit, viral vector, live attenuated, toxoid, mRNA offer tailored approaches to eliciting immune responses against specific pathogens. Each category is defined by its method of action, immunogenicity, safety profile, and suitability for particular populations, such as immunocompromised individuals or young children. The historical trajectory of vaccines demonstrates an accelerating pace of innovation. Beginning with Edward Jenner's smallpox vaccine in 1796, through the 20th-century advancements like polio and MMR vaccines, to the global mobilization against COVID-19, vaccines have evolved alongside scientific progress. Their development has been supported by global institutions like the WHO and fueled by increasing knowledge in microbiology, immunology, and genetic engineering. Integral to the success of modern vaccines are delivery systems and carriers that enhance efficacy and stability. Lipid Nanoparticles (LNPs), viral vectors, and protein carriers play vital roles in ensuring that vaccine components reach target cells effectively and stimulate robust immune responses. Additionally, innovative delivery formats such as microneedle patches and oral vaccines hold promise for expanding access and improving compliance, particularly in low-resource settings. Adjuvants like aluminum salts and newer emulsions further amplify the immune system's response to antigens, making vaccines more effective, especially in populations with weaker immune reactions. mRNA technology has emerged as a groundbreaking tool with broad implications. Initially hindered by instability, synthetic mRNA has become viable through structural modifications and LNP encapsulation. The rapid development and deployment of mRNA COVID-19 vaccines have proven their efficacy and adaptability. Unlike traditional vaccines, mRNA platforms offer speed, flexibility, and scalability, allowing for rapid responses to emerging pathogens. Moreover, they do not carry the risk of infection or genomic integration, making them safer alternatives for widespread use. Despite their success, mRNA vaccines face challenges such as cold-chain storage requirements, durability of immunity, and vaccine hesitancy. Addressing these issues is essential for global vaccine equity and long-term public health success. Furthermore, the application of mRNA extends beyond infectious disease, showing potential in cancer immunotherapy and genetic disorder treatments. Personalized mRNA cancer vaccines and gene replacement therapies represent promising frontiers, offering new hope for previously untreatable conditions. In nutshell, vaccines are a cornerstone of modern medicine, reflecting centuries of scientific progress and public health collaboration. The integration of new technologies such as mRNA into vaccine development has redefined possibilities in both preventive and therapeutic medicine. As the world continues to face evolving health threats, sustained investment in vaccine research, equitable distribution, and public education will be crucial. The future of medicine lies in harnessing the full potential of these innovations while ensuring access for all.

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CONFLICTS OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

mRNA: Messenger Ribonucleic Acid; **LNPs:** Lipid Nanoparticles; **COVID-19:** Coronavirus Disease 2019; **IPV:** Inactivated Poliovirus Vaccine; **OPV:** Oral Poliovirus Vaccine; **WHO:** World Health Organization; **MMR:** Measles, Mumps, and Rubella (vaccine); **HPV:** Human Papillomavirus; **SARS-CoV-2:** Severe Acute Respiratory Syndrome Coronavirus 2; **BCG:** Bacillus Calmette–Guérin (vaccine); **PCV13:** 13-valent Pneumococcal Conjugate Vaccine; **HBsAg:** Hepatitis B Surface Antigen; **VLP:** Virus-Like Particle; **ChAdOx1:** Chimpanzee Adenovirus Oxford 1 (viral vector platform used in vaccines like AstraZeneca's COVID-19 vaccine); **MHC:** Major Histocompatibility Complex; **Hib:** Haemophilus influenzae type b; **AS03:** Adjuvant System 03 (an oil-in-water emulsion adjuvant); **MF59L:** An oil-in-water emulsion adjuvant used in vaccines; **DNA:** Deoxyribonucleic Acid; **CMV:** Cytomegalovirus.

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