Review Article

Recent Advances in Vaccines and Immunotherapy Techniques in Pharmacological Perspectives

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ABSTRACT

Recent advances in vaccines and immunotherapy have transformed disease prevention and treatment paradigms globally. Vaccines, biological preparations containing weakened or inactivated pathogens or their antigens, stimulate immune memory and provide prophylactic protection, having saved millions of lives by controlling infectious diseases such as smallpox, polio, and rabies. Modern vaccine technologies now include mRNA vaccines, viral vector vaccines, oral and needle-free delivery systems, and plant-based edible vaccines, each addressing specific challenges of stability, delivery, and immune response enhancement. mRNA vaccines, exemplified by COVID-19 vaccines, enable rapid, flexible design and safe immunization by instructing host cells to produce antigenic proteins, accelerating response to emerging diseases. Viral vectors offer targeted antigen delivery but face immune pre-existing immunity hurdles addressed by novel adenovirus serotypes. Oral and edible vaccines promise easy administration and global accessibility, overcoming cold chain limitations. Immunotherapy harnesses the body's immune system to combat cancer and autoimmune diseases, employing monoclonal antibodies, CAR-T cells, checkpoint inhibitors, and cancer vaccines. These advance precision medicine by targeting tumor-specific antigens and restoring immune balance. Despite dramatic progress, challenges remain including high costs, safety concerns, adverse effects, and logistical hurdles such as mRNA vaccine storage. Emerging fields such as personalized cancer immunotherapy and integration of artificial intelligence and nanotechnology in vaccine development show considerable promise for enhancing therapeutic efficacy, design speed, and delivery. This comprehensive review highlights the evolving landscape of vaccine and immunotherapy innovations, their clinical applications, and future prospects, reinforcing their critical role in global health management and personalized medicine.

Keywords: Vaccines, Immunotherapy, mRna vaccines, Viral vector vaccines, Cancer immunotherapy, Personalized medicine.

INTRODUCTION

1.1. Basics of vaccines and immunotherapy :

According to WHO, approximately 1.5 million children below age 5 still die due to lack of childhood vaccines. Major pathogens, including smallpox, polio, and rabies, that killed hundreds of millions of individuals in the last few centuries are largely under control because of the availability of safe and effective prophylactic vaccines. Vaccines have been successful in eradicating many childhood-related infections and saved 10 million lives between mid-1960 and 2015 with viral vaccines[1]. Vaccines are biological preparations that enhance immunity against a particular disease. A vaccine contains an agent that resembles a disease-causing microorganism and is often made from weakened or killed forms of the microbes, their toxins, or one of their surface proteins. This agent stimulates the body's immune system and recognizes the agent as a foreign particle, destroys it, and keeps the record of it because when the same agent enters into the body, the immune system easily recognizes and destroys later encounters. The word "vaccine" is derived from the Latin word "vacca," which means "cow." The first vaccine was developed by Edward Jenner in the late 18th century. He developed the successful vaccine for smallpox in 1796. He named the method "vaccination" because it uses material derived from cowpox. Vaccines do not guarantee complete protection from diseases[2]. The material used for the smallpox vaccine is from the lymph of the cow. After vaccinating the cow with cowpox matter, the lymph is collected from the cow. In India, the first doses of smallpox vaccine lymph arrived in 1802. The first person to receive the smallpox vaccine was a three-year-old child from Bombay on June 14, 1802[3]

Table 1: Vaccines and their route of administrations.

Name of the vaccine	Route of administration
Measles, Mumps, and Rubella (MMR)	Subcutaneous injection
Oral Polio Vaccine (OPV)	Oral
Yellow Fever	Subcutaneous injection
Rotavirus	Oral
Varicella (Chickenpox)	Subcutaneous injection
Bacillus Calmette-Guérin (BCG)	Intradermal injection
Nasal Influenza Vaccine (LAIV)	Intranasal spray
Hepatitis A and B vaccine	Intramuscular
Human papillomavirus (HPV)	Intramuscular
Haemophilus Influenza type-B(HIB)	Intramuscular[4].
Small pox (vaccinia) vaccine	Percutaneous
Dengue Tetravalent vaccine	Subcutaneous
Ebola Zaire Vaccine	Intramuscular
Rotavirus Vaccine	Oral
SARSCOV-2(JanseenCovid-19 vaccine)	Intramuscular[5].

1.2 Immunotherapy:

Immunotherapy is a type of medical therapy that uses patients' natural immune systems to fight against infectious diseases and cancer. Instead of destroying patients' cancer cells directly, immunotherapy trains patient's immune systems to recognize cancer cells and selectively target and destroy the[6]. Cancer immunotherapy is used as a beneficial tool in cancer treatment by stimulating the immune system to produce antitumor effects. Immunotherapy was first introduced by Dr. William B. Coley in 1891. He was an American bone surgeon. He is recognized as the FATHER OF CANCER IMMUNOTHERAPY. He made the first attempt to stimulate the immune system for improving a cancer patient's condition by intratumorally injecting in activated bacterial toxin[7]. Intravenous immunoglobulin (IVIG) (a treatment made from antibodies) can be given through a vein at 0.4 g per kilogram of body weight for 5 days to treat Guillain–Barre syndrome. However, the amount used can change depending on the disease. Low doses of cyclophosphamide affect the immune system's cell-based defences more strongly. In people, a single low dose of 600 mg per square meter of body surface area lowers B-cell numbers more than T-cell numbers. Among T-cells, the CD8 type drops more than the CD4 type.

• Some of the adverse effects of immunotherapy include:

- Cyclophosphamide and chlorambucil can damage the bone marrow, so white blood cell counts need to be checked regularly.
- Azathioprine lowers both T-cells and B-cells.
- Transfer factor should be given carefully to people with Type I allergies, because it can cause a severe allergic reaction.
- Interleukins should be given in small doses to avoid side effects and reduce illness.
- Glucocorticoids (steroid medicines) can cause bone loss (osteoporosis) by affecting calcium balance. They can also increase appetite, cause fat buildup around the stomach and face, slow wound healing, raise the risk of infection, suppress hormone production, and stop growth in children. Other side effects include muscle weakness, bone death from poor blood flow (avascular necrosis), high blood pressure, flushed face, high cholesterol, and swelling.
- NSAIDs (pain and inflammation medicines) can cause stomach irritation, ulcers, kidney problems, confusion, memory loss, and personality changes, especially in older people[8].

1.3 Importance of modern medicine:

Modern medicine is also known as allopathic medicine, conventional medicine or western medicine. Allopathic medicine is a way of treating illnesses using methods that have been tested and proven by science. It is based on knowledge about how the body works, including biology, anatomy, and chemistry. It mainly uses medicines, surgery, and other medical procedures to cure diseases or reduce symptoms. The word "allopathy" was first used by Samuel Hahnemann, who started homeopathy. He used it to describe treating diseases by creating effects that are the opposite of the symptoms. Over time, allopathic medicine changed a lot, using new scientific discoveries, and it became the main type of medicine used around the world[9]. The biggest advantage of modern medicine is that it is based on evidence-based system This means every test and treatment is backed by strong research.

• Other benefits include:

- Care from well-trained and licensed doctors.
- Access to the best medicines.
- Use of advanced testing and scanning machines.
- Treatments that have been carefully studied and tested.
- Clinics and hospitals available in most places[10].

2.TYPES OF VACCINES:

Table 2: Types of vaccines with Licensed Examples, MOA and Uses

Vaccines	Licensed vaccine using this technology	Year	Mechanism of action	Uses
Inactivated vaccines	• Flu • Polio • Rabies • Hepatitis A • Influenza	1885[11],	After vaccination, the antigen is taken up by an antigen-presenting cell (APC). The APC carries the antigen to a nearby lymph node The APC places a piece of the antigen (epitope) on its surface with an MHC molecule. This allows the APC to interact with and activate T cells Helper T cells then stimulate either an antibody response or a cell-mediated response.	Inactivated vaccines are valued for their reduced production costs. They provide increased vaccine safety compared to live vaccines. They allow for relatively straightforward upscaling during vaccine production. Inactivated vaccines have been used for more than 100 years to protect people from viral diseases[13].

			The immune system builds memory cells, so it can react faster and stronger if the pathogen appears again[12].	
Mrna vaccine	• Pfizer-BioNTech • COVID-19	1961[14].	The vaccine delivers mRNA into the body's cells. This mRNA gives instructions to the cells to make a viral protein. In COVID-19 vaccines, the protein made is the spike protein of SARS-CoV-2. The immune system detects this protein as something foreign. It reacts by producing antibodies and training immune cells. Later, if the real virus infects the body, the immune system can respond quickly and protect against illness[15].	Safe vaccination: since they are non-infectious, they can be used without risk of causing disease. Genetic safety: useful because they do not integrate into the human genome. Temporary action: designed for short-term presence in the body, making them safer for repeated use. Wide accessibility – suitable for people with egg allergies or where cell-based production is not feasible. Rapid response – can be applied in outbreak or pandemic situations due to fast and scalable manufacturing. Immune system activation – used to stimulate the innate immune response, providing early defense. Long-term protection – applied to induce T-cell and B-cell responses, creating both cellular and antibody immunity[16].
Live-attenuated vaccines	• Chicken pox • Measles • Mumps • Rubella	1892	Administration -The weakened (attenuated) germ is given to the body, usually by injection, orally, or through a nasal spray. Replication – Once inside, the germ starts to multiply, but much more slowly and weakly than the normal disease-causing germ. Innate Immunity Activation – Immune cells (macrophages, dendritic cells) detect the germ through special sensors. They release signals (cytokines, chemokines) that cause inflammation and call other immune cells to help. Antigen Presentation: Dendritic cells carry pieces of the germ (antigens) to the lymph nodes and show them to T cells and B cells, starting a targeted immune response. Antibody Response: B cells turn into plasma cells that make antibodies. These antibodies block the germ from entering cells and mark it for destruction. Cell-Mediated Immunity: T cells are also activated. Killer T cells destroy infected cells, while Helper T cells release signals that boost the overall immune response. Memory Formation: Some B and T cells become memory cells. These stay in the body for years or even a lifetime. Protection: Because of both antibodies and memory cells, the body can react quickly if the real germ comes later, often preventingsickness altogether[17].	Strong Immunity: These vaccines give powerful and long-lasting protection. Additional doses, or booster shots are not always needed. Natural-like Protection: Since the weakened germ can still multiply, it acts like a natural infection and builds full immune defines, including body and mucosal immunity Cost-effectiveness: Live attenuated vaccines are often low-cost and may require fewer doses. Herd Immunity: They help protect the whole community, even people who can't take the vaccine. These vaccines have proven remarkably effective against a wide range of infectious diseases like measles, mumps, rubella, varicella, rotavirus[18].

Toxoid vaccines	• Tetanus • Diphtheria • Pertussis	1923	When a toxoid vaccine is given, special immune cells called antigen-presenting cells (APCs), like dendritic cells, take in the toxoid. These cells break down the toxoid into smaller parts (peptides). The peptide pieces are displayed on the surface of APCs using Major histocompatibility complex class-2 (MHC-II) molecules. This display activates CD4+ T cells (helper T cells), which then release signals (cytokines) and help B cells As a result, B cells turn into plasma cells that make antibodies and become memory B cells for long-term protection[19].	Toxoid vaccines work well against diseases caused by toxins, like tetanus, diphtheria, and pertussis Non-virulent – Toxoid vaccines are made from inactivated toxins, so they cannot cause disease. Stable – They remain effective and do not easily lose their potency. Long-lasting in storage – Toxoid vaccines can be stored for long periods without losing effectiveness[20].
Subunit vaccines	• Shingles • Hepatitis B • Acellular pertussis • Pneumococcal[21].	1981	Polysaccharide Component – The vaccine contains a sugar (polysaccharide) from the surface of the bacteria. Conjugation with Protein – This sugar is chemically linked (conjugated) to a protein. Improved Immune Recognition – The protein helps the immune system recognize and respond strongly to the bacterial sugar. Stronger Memory Formation – The conjugation allows the immune system to form long-term memory against the bacteria. Future Protection - If the person is exposed to the bacteria later, the immune response will be quicker and more effective[22].	Disease prevention – They are used to prevent infectious diseases like hepatitis B, HPV, and whooping cough(pertussis), HIB, pneumoniae, Meningitis, blood Stream infectious. Safe for weak immunity – Can be safely given to immunocompromised people since they don't contain live pathogens. Targeted protection – Provide immunity against specific parts (antigens) of a pathogen that trigger a strong immune response. Reduced side effects – Because they only contain selected fragments, the chances of causing adverse reactions are lower[23].
Conjugate vaccines	• Haemophilus Influenza type b(Hib) • Salmonella typhi • AS typhi • Neisseria Meningitis[24].	1985[25]	Subunit vaccines are made from small parts of the pathogen, like proteins or sugars. These parts are specially chosen to create a strong and useful immune response Since only limited parts of the pathogen are used, the chance of side effects is low. The vaccine trains the immune system to detect and fight these antigens. It also builds memory in the immune system, so future infections are recognized and fought quickly[26].	Conjugate vaccines are used to protect against Streptococcus pneumoniae infections. They help prevent diseases caused by Neisseria meningitidis. They are also used to protect against Haemophilus influenzae infections, reducing illness and death worldwide[27].
D.N.A vaccines	• Zycov-d (Zydus Cadila) • West Nile[28].	2005[29]	Delivery: Plasmid DNA is injected into muscle or skin cells. Antigen production: Host cells produce the encoded antigen protein. Antigen presentation: Released antigens are captured by APCs presented on MHC -I activates $CD8^+$ T cells (cross-priming). DNA can directly enter APCs antigens presented on MHC I & II activates $CD8^+$ and $CD4^+$ T cells. Humoral immunity: B cells capture antigens produce antibodies. Innate immunity activation:	DNA vaccines can create both antibody (humoral) and T-cell (cellular) immune responses, which help the body fight the virus effectively. They are easy and quick to design and produce in large amounts, making them useful for fast response during pandemics. They can be changed easily to include genes from new variants of the virus, which helps in making vaccines against emerging strains. DNA vaccines are stable at room temperature for long periods, so they

			CpG motifs in plasmid DNA activate TLR9 and cytosolic DNA sensors (STING: TBK1 pathway) cytokine and interferon production[30].	are very useful in countries without advanced cold storage systems. They are cost-effective to make and distribute, making them practical for large-scale immunization programs[31].
Viral vector vaccines	• Covishield • Janssen (Ad26.Cov2. S) • Sputnik • Convidice.[32]	2019[33].	After injection, the vaccine viruses enter human cells and insert their genetic material, including the antigen gene, into the nucleus. Human cells then produce the antigen as if it were one of their own proteins. The antigen is displayed on the cell surface along with other proteins. Immune cells detect this foreign antigen and trigger an immune response. B cells produce antibodies, while T cells attack infected cells. T cells check the proteins on cell surfaces; in future if they see a foreign antigen, they destroy that cell[34].	Viral vector vaccines are used because they are safe and provide stable immune protection. They are used to produce a strong immunogenic response. They are used to generate humoral immunity by producing antibodies. They are used to induce cell-mediated immunity through T-cell activation. They are used to stimulate mucosal immunity at entry sites like respiratory and gut surfaces. They are used to provide immunity against pathogens using viral vectors as carriers[35].

3. RECENT ADVANCES IN VACCINE DEVELOPMENT:

3.1 mRNA vaccines:

Progress, however, was slow at first. Early attempts faced major hurdles: mRNA was unstable, broke down quickly in the body, and was easily destroyed by enzymes. Its large size and negative charge made it difficult to cross cell membranes, and delivering it effectively into dendritic cells often required special injection methods. Although adding adjuvants could boost the immune response, this came at the cost of reduced protein production. These challenges, combined with concerns about safety and poor delivery inside the body, initially limited investment and slowed development[36]. mRNA vaccines are scalable but still require advanced technology, making them more costly to produce than traditional vaccines. Their success against COVID-19 has accelerated research into new uses, including vaccines for malaria, HIV, and tuberculosis-diseases that have been tough to control with older methods. Scientists are also developing personalized mRNA cancer vaccines designed to target specific tumor markers in individual patients. This technology has transformed immunization by enabling faster, more effective responses to infectious diseases. Unlike traditional vaccines that rely on weakened or inactivated viruses, mRNA vaccines instruct the body's own cells to make proteins that spark an immune response[37]. Over time, scientists found solutions. Nucleotide modifications and improved mRNA designs made the molecules more stable, and new non-viral delivery systems offered safer and more effective ways to get mRNA into cells. Researchers persisted because of mRNA's safety, simple design, and easy manufacturing. This persistence paid off with the creation of highly effective COVID-19 vaccines, which became a crucial tool in the pandemic response. Today, mRNA vaccine development has a strong framework, covering design, synthesis, and delivery technologies, and continues to expand into new medical applications[38].

E.g., Pfizer-BioNTech, Moderna for COVID-19.

3.2 Viral vector vaccines:

The idea of using viruses as carriers for foreign antigens began to take shape in the 1980s. Early studies showed that recombinant poxviruses, especially vaccinia, could protect animals from unrelated pathogens. This was a major proof of concept for vector-based vaccines. Poxviruses were particularly promising because they could carry large amounts of genetic material without losing their ability to replicate or stimulate immunity. The global eradication of smallpox through widespread vaccinia vaccination further proved the safety and effectiveness of this approach. Afterward, researchers developed safer derivatives like Modified Vaccinia Ankara (MVA), which kept the strong immune response of vaccinia but was more attenuated and safer. In the late 1990s and early 2000s, adenovirus vectors became popular. They were easy to engineer, produced high levels of proteins, and generated strong T-cell responses. Early HIV vaccine trials highlighted these strengths, but the STEP trial revealed a major challenge: many people already had immunity to Ad5, which reduced the vaccine's effectiveness. This problem led scientists to test other adenovirus types, such as Ad26 and Ad35, as well as nonhuman adenoviruses like chimpanzee-based ChAdOx1. Around the same time, researchers also studied other viral vectors including vesicular stomatitis virus (VSV), alphaviruses, measles virus, and lentiviruses each offering unique benefits. For example, alphaviruses can self-amplify to boost antigen expression, while lentiviruses provide long-lasting antigen production and strong T-cell activation, making them useful for therapeutic vaccines. A major milestone came with the approval of the rVSV-ZEBOV

vaccine against Ebola, which showed that viral vectors could be used safely and effectively in outbreak situations. Later, during the COVID-19 pandemic, adenovirus-based vaccines were rapidly developed, authorized for emergency use, and delivered to hundreds of millions of people worldwide. Together, these breakthroughs demonstrate the flexibility and potential of viral vector vaccines in tackling both ongoing and emerging health threat[39].e.g., Covishield, J&J.

3.3 Needle -free and oral vaccine delivery system:

One of the most well-known examples of a needle-free vaccine that has been used for decades, administered orally, rather than by injection. The first oral vaccine was introduced in the 1960s, with the oral polio vaccine (OPV) being the first to demonstrate proven effectiveness. Since then, OPV has remained in use across many countries worldwide as a crucial tool for preventing polio. Oral vaccines function by delivering antigens through the gastrointestinal tract, which stimulates an immune response similar to that of traditional injectable vaccines. Early on, however, this method faced challenges. The intestinal lining had a limited capacity to present antigens and induce strong immunity, and large amounts of antigen were required to achieve protection, making oral vaccine production and distribution more difficult. Over time, advancements in medicine and molecular biology have transformed this field. Researchers have developed strategies to enhance the presentation of antigens within the gut, strengthening immune responses and improving tolerance to oral vaccines. These scientific improvements have not only increased the effectiveness of oral immunization but have also expanded its potential applications. Oral vaccines are now better able to address both practical barriers, such as manufacturing and dosage requirements, and biological barriers, such as weak mucosal immunity. Importantly, oral vaccines also offer protection against pathogens that enter through the intestinal lining and cause systemic diseases, such as Salmonella enterica serovar Typhi and poliovirus. With the rapid pace of scientific innovation—accelerated by the global focus on vaccine development during the COVID-19 pandemic—progress in this area has been substantial. Modern technologies are enabling the design of safer, more efficient, and more widely accessible oral vaccines, marking a significant shift from their early limitations to their growing role in global disease prevention[40].

3.4 Plant -based or edible vaccines:

The concept of edible vaccines emerges in 1990, when a patent application under the International Patent Cooperation Treaty reports the first case of expressing a surface protein from Streptococcus in tobacco leaves at a level of about 0.02% of total leaf protein. Around this time, Dr. Charles Arntzen conceives the revolutionary idea of edible vaccines and begins to push it toward realization. By 1992, Arntzen and his collaborators introduce the concept of using transgenic plants as both a production platform and a delivery system for subunit vaccines. In this approach, the edible parts of genetically modified crop plants serve as the carriers of antigenic proteins. This breakthrough addresses several of the limitations faced by traditional vaccines, such as high production costs, the need for refrigeration, and complicated delivery systems, and it triggers a wave of global research interest in edible vaccine technology. During the 1990s, the expression of the Streptococcus mutans surface protein antigen A in tobacco becomes the first milestone achievement in this field. The same group of pioneer scientists furthered work by expressing antigens for hepatitis B and the heat-labile toxin B subunit in both tobacco plants and potato tubers. These experiments demonstrate that staple crops can successfully produce medically important proteins within their tissues. At the same time, researchers show for the first time that transgenic tobacco plants are able to express the hepatitis B surface antigen (HBsAg), providing strong evidence that plants can act as biofactories for vaccine production. This combination of proof-of-concept studies establishes the foundation for using plants as safe, scalable, and cost-effective vaccine platforms. To validate the effectiveness of this approach, researchers test whether plant-derived HBsAg is capable of stimulating mucosal immune responses when consumed orally. For this purpose, potato tubers are chosen as the expression system, since they can be eaten directly without extensive processing. Scientists work on optimizing the expression to increase the accumulation of the antigen within potato tissues, making them a practical vehicle for vaccine delivery. These successful demonstrations not only confirm that edible plant tissues can provoke an immune response in the body but also highlight the immense potential of edible vaccines in global healthcare. Today, the concept continues to expand as researchers explore a wide range of plant systems, from cereals to fruits, aiming to develop cost-effective, needle-free vaccines for infectious diseases worldwide[41].

4. RECENT ADVANCES IN IMMUNOTHERAPY:

4.1 Monoclonal antibodies:

Monoclonal antibodies are a remarkable breakthrough in biomedical science and have changed the way many diseases are treated. These monoclonal antibodies are made from identical copies of a single immune cell, allowing them to target specific antigens with great precision. This makes them incredibly useful in treating conditions such as cancer, autoimmune disorders, and infectious diseases. The process of creating monoclonal antibodies was first developed by scientists Georges Köhler and César Milstein in the 1970s. Their method involved fusing a specific B cell that produces an antibody with a cancer cell, creating a hybridoma. This hybrid cell could produce an endless supply of the antibody, which is then isolated and purified for use in therapies, diagnostics, and research. In recent years, monoclonal antibodies have become essential in the treatment of various diseases. In oncology, they help by targeting cancer cells directly, which reduces the risk of damage to healthy cells, making treatment more precise. For infectious diseases, monoclonal antibodies can neutralize harmful pathogens or their toxins, offering a

highly targeted way to fight infections. In autoimmune conditions, they can either suppress an overactive immune system or boost immunity in situations where it is needed. However, the production of these antibodies is complex and costly, and they can sometimes cause side effects, such as immune reactions. Despite these challenges, advances in biotechnology are continually improving their effectiveness and reducing their production costs. Monoclonal antibodies are made of two main parts: the Fab region, which binds to the target antigen, and the Fc region, which triggers the immune system's response. The structure consists of two light and two heavy chains linked by disulfide bonds, providing stability. The heavy chains contain three constant domains and one variable domain, while the light chains consist of one constant and one variable domain. The Fab region is formed by the combination of the variable parts of the heavy and light chains, and the Fc region is made up of the constant parts of the heavy chains. Additionally, post-translational modifications like glycosylation can occur in the Fc domain, affecting how the antibody interacts with the immune system. This structural complexity is part of what makes monoclonal antibodies such powerful and versatile therapeutic tools[42].E.g., Rituximab, Trastuzumab.

4.2 CAR-T cell therapy:

CAR T cell technology was first introduced in 1993 by Zelig Eshhar and his team. They genetically modified T cells to express chimeric genes; a combination of antibody fragments (single-chain antibodies) fused to a transmembrane domain and an intracellular signalling domain from the T cell receptor. This modification allowed T cells to recognize and kill cells that displayed a specific antigen targeted by the antibody. Later studies showed that human T cells engineered with a CD19-specific CAR could effectively eliminate lymphoma and leukaemia cells in immunodeficient mice. In 2010, a case report provided promising evidence that CD19 CAR T cells could successfully treat a patient with lymphoma. Since then, CAR T therapy has delivered remarkable results in patients with relapsed or treatment-resistant B cell cancers, including both acute and chronic lymphocytic leukaemia. Researchers have also tested CAR T cells against solid tumors, but so far, the outcomes have been less effective compared to blood cancers. Using CD19 as a model, Michel Sadelain has published a detailed review that covers the evolution of CAR technology, its clinical success in B cell cancers, the challenges and side effects associated with treatment, and what has been learned from the CD19 CAR T cell experience[43].leukaemia, lymphoma.

4.3 Checkpoint inhibitors:

Immune Checkpoint Inhibitors (ICIs) are a type of cancer immunotherapy that enhance the immune system's ability to fight cancer by targeting specific receptors on T-cells. ICIs became a game-changer in cancer treatment starting in 2011 with the approval of ipilimumab, which revolutionized treatment by offering long-lasting results and lower toxicity in some cases. Unlike traditional treatments, ICIs work by stimulating the immune system to attack tumor cells. Immune checkpoints are mechanisms that maintain a balance between pro-inflammatory and anti-inflammatory signals in the body. These checkpoints are pathways that regulate immune cell activity, either activating or inhibiting immune responses. The most common ICIs target immune inhibitory receptors such as CTLA-4, PD-1, and PD-L1, which have been key in the last decade of immunotherapy research. In addition to these, several other immune checkpoint inhibitors are currently being developed, targeting proteins like B7H3, CD39, CD73, the adenosine A2A receptor, and CD47. New research has also uncovered additional targets, including LAG-3, TIM-3, TIGIT, and VISTA. These studies suggest that blocking one immune checkpoint might trigger compensatory changes, such as the upregulation of other checkpoints in the tumor microenvironment (TME). For example, in lung cancer, the relationship between TIM-3 and PD-1 showed a compensatory mechanism when one was blocked[44].Eg: PD-1, CTLA-4 blockers.

4.4 Cancer vaccines:

Cancer immunotherapy aims to activate the immune system to identify and eliminate cancer cells. They're categorized into passive and active types based on how they stimulate the immune system. Passive immunotherapy includes treatments like tumor-targeting monoclonal antibodies (mAbs) and adoptively transferred T-cells, which have direct anticancer effects. On the other hand, active immunotherapy involves methods like cytokines or checkpoint inhibitors that boost the immune system without specific targeting of the tumor. These treatments are more generalized and rely on activating broad immune responses. Tumor-targeting mAbs are considered antigen-specific because they focus on identifying and attacking cancer cells directly. Cancer vaccines have been proposed as a way to activate the immune system against minimal residual disease after surgery, aiming to prevent or delay recurrence. Most clinical trials have been conducted in late-stage cancers with a large tumor burden, particularly after standard treatments have failed. Success largely depends on overcoming immune suppression caused by the tumor, therapy, or aging. The melanoma vaccine has seen the most success so far, beginning with vaccines made from tumor cell lysates combined with adjuvants. In phase I and II trials, one vaccine, Melacine, showed modest success with a 10-20% response rate in clearing metastatic sites and stabilizing disease. Although it did not outperform chemotherapy in phase III trials, Melacine was non-toxic, offering a better quality of life. It is available in Canada and awaiting approval in the U.S. A similar vaccine, Canvaxin, showed a small but statistically significant improvement in survival rates among stage IV melanoma patients, and a multi-center phase III trial is ongoing[45].Eg: HPV vaccine for cervical cancer.

5.APPLICATIONS IN DISEASES:

5.1 Cancer: Natural killer (NK) cell immunotherapy has been shown to reduce circulating tumor cell (CTC) numbers in cancers such as non-small cell lung cancer (NSCLC) and hepatic carcinoma, with a decrease in CTC count correlating

with tumor shrinkage. Combination therapies, including irreversible electroporation (IRE) combined with NK cells, demonstrate that CTC numbers reflect treatment efficacy in unresectable liver cancer. PD-L1 expression on CTCs offers a non-invasive alternative to tissue biopsy for assessing patient eligibility for immunotherapy, overcoming the risks and limitations associated with traditional biopsies. Patients with PD-L1-positive CTCs prior to PD-1 inhibitor treatment often have poorer outcomes, whereas those with PD-L1-negative CTCs generally respond better to therapies such as nivolumab. The presence and PD-L1 status of CTCs also predict progression-free survival across cancers like head and neck and gastrointestinal tumors. Monitoring dynamic changes in PD-L1-positive CTCs during treatment provides valuable insight into immunotherapy response. Additionally, expression of melanoma-associated markers such as MART-1, MAGE-A3, and PAX3 on CTCs correlates with prognosis and helps guide immunotherapy strategies in melanoma patients[46].

5.2 Autoimmune diseases:

Autoimmune diseases develop when the immune system mistakenly attacks the body's own healthy tissues, causing chronic inflammation, pain, and organ or joint damage. Immunotherapy plays a key role in correcting these faulty immune responses. One important target is the B cell, which is often responsible for producing autoantibodies that contribute to disease progression. Monoclonal antibodies, such as rituximab, are used to eliminate B cells and reduce this harmful autoantibody production. Another effective strategy involves checkpoint inhibitors, which block immune signals like PD-1 and CTLA-4 to rebalance overactive T-cell responses. These agents help reduce immune system attacks in conditions such as lupus and rheumatoid arthritis. In addition, T-cell therapies are designed to selectively remove or suppress harmful T cells while preserving healthy immune function. Because these treatments are highly targeted, they often result in fewer side effects compared to traditional immunosuppressants. Overall, immunotherapy restores immune balance and offers long-term benefits in managing autoimmune diseases and improving patient quality of life[47].

5.3 COVID-19:

Immunotherapy for COVID-19 involves the use of monoclonal antibodies (mAbs) that target the spike (S) glycoprotein of SARS-CoV-2. These antibodies are designed to block the virus from entering human cells. The spike protein normally binds to ACE2 receptors on host cells to initiate infection, but mAbs prevent this crucial interaction. In addition, the host cell protease TMPRSS2, which facilitates viral entry, is also disrupted indirectly by mAb action. By preventing viral entry, mAbs effectively stop the virus from replicating and spreading throughout the body. Unlike vaccines that take time to generate immunity, mAbs provide immediate passive protection. They can be used as pre-exposure or post-exposure prophylaxis, as well as during active infection. This form of immunotherapy is especially important for high-risk individuals, including the elderly, obese, diabetics, and those with cancer or chronic lung conditions. It also serves as an alternative for people who are unable to receive COVID-19 vaccines. The use of mAbs should be based on a personalized risk-benefit analysis. Although their protection is temporary, monoclonal antibodies offer critical short-term immunity lasting for several weeks or months[48].

6.CHALLENGES AND LIMITATIONS:

6.1 High cost of immunotherapy:

Cancer immunotherapy has brought major improvements in survival and quality of life for cancer patients. However, these treatments come at a very high cost, raising serious concerns about the long-term sustainability of healthcare systems. In 2014, the U.S. alone spent $42.4 billion on oncology drugs. Immune checkpoint inhibitors like nivolumab and pembrolizumab have shown strong results in treating melanoma (MM), non-small cell lung cancer (NSCLC), and renal cell carcinoma (RCC), leading to their evaluation in other types of cancer. While these expanded uses are promising, the financial burden could become overwhelming.

A 2016 study looked into the one-year costs of these drugs. Pembrolizumab costs $145,010 per patient for MM and $130,511 for NSCLC, offering a median progression-free survival (PFS) of 6.3 months for both. The global one-year cost of pembrolizumab was $3.8 billion for MM and $83.9 billion for NSCLC. Nivolumab, on the other hand, had lower per-patient costs: $64,680 for MM and $44,100 for NSCLC, with median PFS of 5.1 months and 3.5 months, respectively. Its worldwide costs reached $1.7 billion for MM and $47.2 billion for NSCLC. The higher global cost for NSCLC treatment is due to its much greater incidence compared to MM. For RCC, nivolumab cost $32,130 per patient per year and provided a median PFS of 4.6 months, totalling $2.7 billion in worldwide spending[49].

6.2 Safety and efficacy of immunotherapy:

In recent years, there has been significant progress in understanding how cancer interacts with the immune system. This growing knowledge has led to the rapid development and integration of cancer immunotherapies into clinical practice. These treatments have shown strong effectiveness in many cases and are particularly appealing because they target cancer cells while minimizing damage to healthy tissues—unlike traditional chemotherapy and radiation, which often cause serious side effects. Previously, only a few immunotherapies showed consistent clinical success, such as high-dose interleukin-2 (IL-2) in treating advanced melanoma and renal cell carcinoma (RCC). However, more recent advancements have greatly improved outcomes, with many patients experiencing positive, and sometimes even complete or long-term, responses—even in aggressive or solid tumors.

Currently, the most successful results have been seen in patients with melanoma, RCC, and certain blood cancers. These cancers respond especially well to immunotherapy.

Still, emerging research suggests that many other types of cancer may also benefit from these treatments in the near future. Overall, cancer immunotherapy is becoming a powerful and promising approach, offering new hope to patients who previously had limited treatment options[50].

6.3 Adverse effects of immunotherapy:

Adverse Event Following Immunisation (AEFI) refers to any unexpected health issue that occurs after a person receives a vaccine, though it doesn't always mean the vaccine caused it. AEFIs can range from mild symptoms like fever or swelling to severe cases such as seizures, coma, or even death. These events can result from the vaccine itself, mistakes in how it's stored or given, or anxiety related to the injection. Vaccines go through strict testing for safety, quality, and effectiveness before they are approved. Because they are given to healthy individuals, people are especially sensitive to any side effects. That's why it's important to tell the difference between a true vaccine reaction and a coincidental health issue.

According to a 2018–2019 GAVI report, fear of side effects was the second leading reason for low vaccine coverage in India, after lack of information. These concerns have remained significant even after the COVID-19 pandemic. Recent studies show vaccine hesitancy in India ranges from 13% to 49% depending on the region, with safety and trust issues being the most cited reasons. National surveys show overall confidence in vaccines, but doubts about side effects persist. The World Health Organization (WHO) oversees the global tracking of serious AEFIs to help detect risks early. In India, a dedicated AEFI committee investigates each reported case to confirm the cause. These steps are crucial to protect public health and maintain trust in immunization programs. Regular analysis of vaccine safety and clear public communication are essential. Transparency helps fight misinformation and reduce fear. An informed public is more likely to accept vaccines. Trust in the system grows when safety concerns are addressed promptly and openly[51].

6.4 Cold chain and storage [for mRNA vaccines]:

mRNA vaccines are known for being effective and safe, but one of their biggest challenges lies in their storage requirements. They are inherently unstable and need to be kept at ultra-cold temperatures to remain effective. Their stability is influenced by various factors, such as pH, temperature, and added ingredients. To protect the mRNA, manufacturers use lipid nanoparticles (LNPs) as carriers. Although all mRNA vaccines use LNPs, the storage needs vary by manufacturer. For instance, the Pfizer-BioNTech vaccine must be stored at −80°C and has a shelf life of six months, while Moderna's vaccine is stored at −20°C but offers the same shelf life. Pfizer also uses special dry ice packaging for safe transport. The stricter storage conditions for Pfizer's vaccine are likely due to added safety precautions rather than differences in the vaccine's makeup.

However, recent data submitted to the European Medicines Agency indicates that Pfizer's vaccine can remain stable for up to 30 days when refrigerated at 2–8°C, similar to Moderna's. These ultra-cold requirements pose significant challenges for vaccine distribution, particularly in low-resource countries. Setting up and maintaining ultra-cold storage is expensive and logistically difficult in many regions. The short shelf life, combined with vaccine hesitancy, has led to large-scale vaccine wastage. In fact, around 50% of vaccines globally are wasted due to poor temperature control. Therefore, a major focus now is on developing thermostable mRNA vaccines that can be stored at standard refrigeration temperatures and distributed more easily and cost-effectively[52].

7.FUTURE PERSPECTIVES:

7.1 Personalized cancer immunotherapy:

Personalized immunotherapy is changing cancer treatment by using precision medicine to design therapies based on each patient's unique tumor. Instead of one-size-fits-all approaches, doctors study the tumor's genes, proteins, and immune features. This helps target specific weaknesses in the tumor, making treatment more effective and reducing side effects. Tools like genomic and proteomic analysis guide these personalized therapies. The goal is to match each patient with the therapy most likely to succeed.

AI and machine learning are making personalized immunotherapy even smarter. Platforms like IBM Watson and Tempus Labs study large amounts of data to predict which treatments will work best for a patient. These tools consider genetics, treatment history, and clinical results to guide decisions. New systems like D-CRAFT aim to offer real-time, tailored suggestions for advanced immunotherapies. This makes choosing the right treatment faster and more accurate.

Biomarkers play a key role in deciding which immunotherapy is best. For example, PD-L1 expression can predict how well checkpoint inhibitors will work. Tumor mutational burden also helps identify likely responders. Since tumors vary within and between patients, understanding this is vital. Advanced profiling helps doctors create flexible treatment plans that evolve over time. The result is safer, more precise cancer care for every individual[53].

7.2 AI and nanotechnology in vaccine design:

Artificial intelligence (AI) is changing how vaccines are developed by making it easier to analyze complex biological data. AI tools can now study large sets of genomic, proteomic, and immune system information more quickly and accurately. When combined with high-throughput technologies like gene sequencing, AI speeds up biomedical research significantly. This powerful combination helps scientists make smarter decisions in less time. AI is now central to many new approaches in vaccine development.

Nanotechnology also plays a key role in advancing modern vaccines and drug delivery systems. At the nano level, materials behave differently—they can be more reactive, stable, and easily controlled. These special properties allow

for highly targeted drug delivery, which means treatments can be more precise and effective. This technology improves how vaccines are delivered in the body, reducing side effects and increasing protection. Researchers are using these tools to create smarter, faster treatments.

Together, AI and nanotechnology are shaping the future of vaccine development. AI improves how we find antigens and predict immune responses, helping design vaccines in real time during disease outbreaks. Nanotech ensures those vaccines are delivered accurately and safely. This powerful combo allows for quicker, large-scale vaccine production during global health crises. As both fields grow, they'll continue to revolutionize how we fight disease. The future of vaccines is smarter, faster, and more effective[54].

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CONCLUSION

Recent advances in vaccines and immunotherapy have revolutionized the landscape of disease prevention and treatment. Innovative vaccine platforms such as mRNA vaccines and viral vectors have enabled rapid development, especially exemplified during the COVID-19 pandemic. These technologies have improved efficacy, safety, and scalability, paving the way for tackling emerging infectious diseases. Needle-free and oral vaccine delivery systems address logistical challenges by enhancing accessibility and compliance, particularly in resource-limited settings. Plant-based edible vaccines offer a promising cost-effective approach, broadening immunization coverage globally. Meanwhile, advancements in immunotherapy, including monoclonal antibodies, CAR-T cell therapy, checkpoint inhibitors, and cancer vaccines, have transformed cancer treatment, offering targeted and durable responses. Personalized immunotherapy leverages genetic and proteomic profiling to tailor treatments, maximizing efficacy and minimizing side effects. Integration of artificial intelligence and nanotechnology further accelerates vaccine design and improves delivery systems, promising a new era of precision medicine. Despite these significant gains, challenges such as high costs, safety concerns, cold chain logistics, and vaccine hesitancy persist. Continued research focusing on stability, safety, and affordability is vital for widespread implementation. Moving forward, combining technological innovations with global health strategies can enhance vaccine coverage, efficacy, and safety. Ultimately, these advances hold great promise for managing infectious diseases, cancer, and autoimmune disorders, underscoring immunotherapy's vital role in future medical breakthroughs and global health security.

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