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A Comprehensive Review on Types of Vaccines: From Classic to Cutting-Edge

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Abstract

Vaccination, one of the most remarkable achievements in the history of medicine, has had a profound impact on public health. Over the centuries, the concept of vaccination has evolved significantly, leading to the development of a diverse array of vaccine types. This abstract provides an overview of the various types of vaccination, from traditional live attenuated vaccines to cutting-edge DNA and mRNA vaccines, highlighting their pros and cons.

Keywords: Vaccine; mRNA vaccine; DNA vaccine; Nanoparticle vaccine

Introduction

Vaccination has played a pivotal role in public health, offering a formidable line of defense against infectious diseases. Over centuries, the concept of vaccination has evolved, leading to a diverse range of vaccines. There are several methods used to produce vaccines. Vaccines can consist of attenuated live viruses, inactivated organisms or viruses, inactivated toxins, or pathogen segments such as subunit and conjugate vaccines. The U.S. Childhood Immunization Schedule now recommends live, attenuated vaccines for measles, mumps, rubella (MMR vaccine), varicella (chickenpox), and influenza (nasal spray form of seasonal flu vaccine). This review provides an overview of different types of vaccination, ranging from conventional live attenuated vaccines to recent advancements in immunology.

Vaccines Live or Attenuated

Live attenuated vaccines employ weakened, yet viable, pathogens. The similarity between these infections and actual infections elicits a robust and prolonged response from the immune system. Two well-known examples of vaccines are the measles, mumps, and rubella (MMR) vaccine and the oral polio vaccine.

There are multiple methods available for the production of attenuated vaccines. The disease-causing virus is commonly transmitted through cell cultures or animal embryos, particularly chick embryos. Chick embryos are utilized for the cultivation of the virus. The virus exhibits enhanced replication in chick cells over successive passages, while its replication efficiency in human cells diminishes. A vaccine-targeted virus can be cultivated in over 200 distinct embryos or cell cultures, undergoing a process known as "passaging." The attenuated virus will eventually exhibit reduced or impaired replication capacity within human cells. Subsequently, it can be employed for vaccine production. Viruses transmitted through non-human hosts generate a modified version that remains recognizable to the human immune system, yet exhibits limited replication capabilities within human hosts. When administered to an individual, the vaccine virus does not undergo significant replication to induce illness. However, it does elicit an immune response,

thereby protecting against future infections.

A concern that warrants consideration is the potential reversion of the vaccine virus to a pathogenic state. During the replication process within the human body, the vaccine virus has the potential to undergo alterations that may enhance its transmissibility. The occurrence of this scenario is improbable due to the limited replication capacity of the vaccine virus. When developing an attenuated vaccine, potential alterations are considered. The oral polio vaccine (OPV), a live vaccine administered orally rather than through injection, exhibits certain mutations that are noteworthy. Instances of vaccine-derived poliovirus (VDPV) leading to paralysis are rare. The use of OPV has been discontinued in the United States due to this reason. The inactivated polio vaccine (IPV) has been included in the Recommended Childhood Immunization Schedule.

Live, attenuated vaccines typically confer longer-lasting protection compared to killed or inactivated vaccines.

Pros [1]**:**
- Live attenuated vaccines confer durable immunity.
- Often, a single dose is sufficient.
- Mimic natural infection, providing strong protection.

Cons [1]**:**
- Not safe for immunocompromised individuals.
- Require refrigeration during storage and transport.

Killed or Inactivated Vaccines

The microorganisms in inactivated vaccinations have been killed, so they cannot cause infection. Vaccines against diseases like polio and hepatitis A are two such examples. Pathogen inactivation, typically through the use of heat or chemical agents like formaldehyde or formalin, is used to create vaccines of this type. The pathogen's ability to replicate is limited without compromising its structure, so the immune system can still recognize and respond to it. As viruses are not typically considered to be live organisms, the term "inactivated" is occasionally used instead of "killed" when referring to vaccines of this type.

Unlike live, attenuated vaccines, which can revert to a more virulent condition capable of generating disease, viruses that have been killed or inactivated are unable to replicate at all. However, it should be noted that inactivated vaccines typically provide protection for a shorter period than live vaccinations and typically require the administration of booster doses to achieve long-term immunity. For example, the inactivated polio vaccine and the injectable seasonal flu vaccine are both examples of killed or inactivated vaccinations that are part of the U.S. Recommended Childhood Immunization Schedule.

Pros [2]**:**
- Safe for most individuals, including those with weakened immune systems.
- No need for refrigeration, facilitating distribution.

Cons [2]**:**
- Often require multiple doses or boosters.
- Immunity may not be as robust or long-lasting as live attenuated vaccines.

Subunit, Recombinant, and Conjugate Vaccines

Subunit, conjugate, and recombinant vaccines target particular components of the pathogen. Recombinant vaccines are creations of genetic engineering, whereas conjugate vaccines amalgamate antigens. Subunit vaccines exclusively comprise vital components. Illustrative instances encompass the recombinant HPV vaccine, the conjugate Hib vaccine, and the hepatitis B vaccine (subunit). These vaccines exclusively comprise fragments of the pathogens they aim to shield against.

Subunit vaccines induce an immune response by employing a portion of the target pathogen. This objective can be achieved by isolating a particular protein from a pathogen and subsequently delivering it as an antigen. Examples of subunit vaccinations are the acellular pertussis vaccine and the influenza vaccine administered via injection.

The development of an extra subunit vaccine variation can be achieved through the application of genetic engineering techniques. The process involves the introduction of a gene encoding a protein used in vaccines into either host-virus or cultivated producer cells. The synthesis of the vaccine protein occurs concomitantly with the replication of the carrier virus or the metabolism of the production cell. The implementation of this approach will result in the production of a recombinant vaccine, in which the produced protein will be acknowledged by the immune system, thereby inducing subsequent immunity against the specific virus. Currently, the United States is implementing the administration of a recombinant vaccine for hepatitis B.

Furthermore, the technique of genetic engineering was employed in the development of the human papillomavirus (HPV) vaccine. There are now two available forms of the HPV vaccine, one protecting against two strains and the other against four strains. Despite the difference in the number of strains covered, all vaccines share an identical production technique, wherein a single viral protein is isolated for each specific strain. Virus-like particles (VLPs) are generated through the expression of these proteins. Despite lacking viral genetic material and being non-pathogenic, these virus-

like particles (VLPs) effectively elicit an immune response that confers protection against human papillomavirus (HPV).

Both recombinant vaccines and conjugate vaccines have a common characteristic in that they consist of two discrete constituents. In contrast, conjugate vaccines are prepared by using pieces derived from bacterial coats. The combination of these coatings, which are covalently attached to a carrier protein, functions as a vaccination. Conjugate vaccines are utilized to induce a consolidated immune response that exhibits greater potency compared to the individual constituent. Typically, the carrier protein generates a vigorous immune response, whereas the presenting bacterial component does not. While the bacterial fragment alone does not possess the ability to cause disease, its combination with a carrier protein can trigger an immune response that confers protection against future infections. Currently, the approach employed for manufacturing vaccinations provided to children for pneumococcal bacterial infections is as follows.

Pros [3]**:**

- Exceptionally safe with minimal side effects.
- Suitable for immunocompromised individuals.
- Fewer side effects compared to whole-cell vaccines.

Cons [3]**:**

- Multiple doses are often required for adequate immunity.
- Immunity may be less potent than live attenuated vaccines.

DNA and mRNA Vaccines

In the year 2020, amidst the ongoing COVID-19 pandemic, various nations, including the United States, engaged in a fervent pursuit to develop a vaccine targeting the SARS-CoV-2 virus, the causative agent responsible for the aforementioned global health crisis. In the United States, the initiative known as "Operation Warpspeed" allocated substantial financial resources to multiple pharmaceutical companies to facilitate the development and commercialization of an effective vaccine. In typical scenarios, the vaccine trials would have been conducted sequentially, using a phased approach (such as phase I, phase II, phase III, etc.). Concurrently, in response to the public health crisis, vaccine trials were conducted in a sequential manner, encompassing phases I, II, and III.

By the conclusion of 2020, two vaccines were granted emergency use authorization in the United States, both of which were developed with messenger RNA (mRNA) technology. A further vaccination is expected to receive authorization in early 2021, utilizing viral vectors as its basis, as will be elaborated upon in the subsequent section. The technology in question employs messenger RNA (mRNA) enclosed within a lipid bilayer. then, the vaccine is administered into the human body, wherein the immune cells of the body internalize the vaccine particles and then express the mRNA. The messenger RNA (mRNA) provides the cellular instructions necessary for the synthesis of a protein that closely resembles the spike protein found on the surface of the coronavirus. Subsequently, the immune cell proceeds to secrete such protein to adjacent immune cells, therefore initiating an immune response characterized by the generation of antibodies and the activation of specialized cells tasked with identifying and eliminating coronaviruses carrying the aforementioned spike protein, as well as any host cells that have been infected.

DNA and mRNA vaccines are revolutionary, using genetic material to instruct the body to produce non-infectious pathogen fragments. Notable examples include the Pfizer-BioNTech and Moderna COVID-19 vaccines.

Pros [4]**:**

- Highly effective at stimulating the immune system.
- Swift development and production for rapid response to emerging threats.

Cons [4]**:**

- Ultra-cold storage requirements can hinder distribution.
- Long-term safety data is still being collected.

Viral Vector Vaccines

A third vaccine for the COVID-19 pandemic was granted authorization for administration in the United States in early 2021. This vaccine utilized a hollowed-out simian adenovirus into which the mRNA encoding a coronavirus spike protein was inserted. Similar to mRNA vaccines, the mRNA contained within the viral vector is introduced into immune cells after their uptake of the simian adenovirus after their recognition of it as a pathogen. Following this, the immune cell generates the spike protein, which initiates the subsequent immune response.

Viral vector vaccines employ harmless viruses to deliver pathogen genetic material, triggering an immune response. The Johnson & Johnson COVID-19 vaccine uses an adenovirus vector.

Pros [5]**:**

- Potential for single-dose vaccination.
- Suitable for a broad population and doesn't require ultra-cold storage.

Cons [5]**:**

- Rare blood clotting events have been associated with some viral vector vaccines.

- Limited data on long-term safety.

Toxoid Vaccines

Toxoid vaccines protect against bacterial toxins rather than the bacteria themselves. They're used for diseases like diphtheria and tetanus. Some bacterial infections are not caused by the bacteria themselves but rather by a toxin they secrete. In the case of tetanus, for instance, the symptoms are not caused by the Clostridium tetani bacteria themselves but rather by a neurotoxin (tetanospasmin) they manufacture. Inactivating the toxin that produces disease symptoms allows for the creation of immunizations against this particular infection. Treatment with a chemical, such as formalin, or by employing heat or other means is used to kill or inactivate organisms or viruses for use in killed or inactivated vaccines.

The term "toxoids" refers to immunizations developed using inactivated toxins. Toxoids are frequently classified separately from killed or inactivated vaccinations since they include an inactivated toxin rather than germs.

Pros [6]**:**
- Effective against diseases caused by bacterial toxins.
- Generally well-tolerated with minimal side effects.

Cons [6]**:**
- Booster shots are often required.
- Limited to diseases caused by bacterial toxins.

Recombinant Vector Vaccines

For over four decades, recombinant viral vectors have been employed to transport antigens derived from particular pathogens [7]. In 1972, the initial viral vector which carried an external gene was derived from the SV40 virus [2]. Subsequently, numerous viruses have been modified into vaccine vectors, incorporating lentiviruses, adenoviruses, poxviruses, vesicular stomatitis viruses, and adenoviruses, to elicit immune responses against the proteins produced by the encoded transgenes. Recombinant vector vaccines deliver pathogen components via vectors that have been genetically modified. Utilizing a vesicular stomatitis virus (VSV) vector, the Ebola vaccine is delivered. A considerable number of vaccines that have received clinical approval continue to rely on conventional live or inactivated forms of pathogen cells or whole viruses; this is especially true of veterinary vaccines [8]. Nevertheless, recombinant vaccines have garnered attention due to the substantial number of challenges resolved by the conventional approach through the implementation of recombinant DNA technologies in vaccinology, as previously mentioned. As a result, there is a current transition in the focus of immunization towards the investigation of this technology.

Pros [7]**:**
- Elicit robust immune responses.
- Potential for broad pathogen targeting.

Cons [7]**:**
- Limited data is available for some recombinant vector vaccines.
- Safety and efficacy may vary among different vectors.

Whole-Cell Vaccines

Whole-cell vaccines are often reserved for the prevention of bacterial illnesses such as whooping cough and typhoid fever. These vaccines include the full pathogen that has been rendered harmless. The efficacy of whole-cell immunization was proven in clinical studies of a smaller scale throughout phases I and II. Whole-cell vaccines are complex mixes of antigens, immunogens, and occasionally adjuvants that can induce robust and protective immune responses. However, in the past three years, several high-profile phase III trials have failed to fulfill the planned objectives [7]. The immune response to vaccination in some cases, such as the whole-cell Bordetella pertussis immunization, goes beyond the pathogen the vaccine was intended for and helps to protect against other clinically relevant diseases. One example of this is the measles vaccine, which was developed to prevent measles [8].

Pros [9]**:**
- Offer robust protection against the targeted pathogen.
- Provide long-lasting immunity.

Cons [9]**:**
- May cause more pronounced side effects than subunit vaccines.
- Safety concerns have led to the development of less reactogenic vaccines.

Therapeutic Vaccines

Therapeutic vaccines are specifically formulated to address established ailments, including chronic infections and cancer. They elicit an immune response that destroys particular cells or pathogens. Conventional vaccines elicit the generation of antibodies, which are immune proteins designed to bind to particular pathogens such as bacteria and viruses. Similarly, therapeutic vaccines inhibit the progression of chronic infections such as HIV or stimulate the immune system to target cancer cells. Therapeutic vaccines, in contrast to conventional vaccines administered before infection for protection against disease, are administered after disease onset to mount a more effective, disease-specific immune response. Therapeutic vaccine development can be divided into two distinct approaches:

- Autologous vaccines represent a form of personalized medicine wherein immune cells or cancer cells are extracted from an individual's body to produce a vaccine tailored to that specific individual.
- Allogeneic vaccines are produced through the modification or harvesting of cells from other organisms or laboratory-grown cells. This methodology is frequently employed in the development of therapeutic vaccines for cancer [10,11].

From these cells, scientists can create different types of therapeutic vaccines with distinct mechanisms of action. These include antigenic vaccines, dendritic vaccines, and DNA vaccines.

Pros [12]**:**
- Potential to revolutionize the treatment of diseases like cancer.
- Personalized treatment based on individual patient profiles.

Cons [12]**:**
- Complex disease processes require individualized approaches.
- Efficacy varies depending on disease type and patient characteristics.

Plant-Based Vaccines

Plant-based vaccines use genetically modified plants to produce vaccine antigens, offering cost-effective and scalable production methods [13]. Plant-derived vaccines are produced by recombinant technology, in which the gene encoding the desired antigen protein is integrated into the plant genome. Agrobacterium tumefaciens is commonly used for gene transfer and transformation [14]. Nowadays, plant biotechnology brings new insight to vaccine research through gene transfer strategies to plants and improvements in amount, isolation and purification, and addition of adjuvant for production of recombinant vaccine antigens in plants [15].

Pros [16]**:**
- Low production costs and scalability.
- Rapid response to emerging pandemics.

Cons [16]**:**
- Regulatory and public acceptance challenges.
- Limited long-term safety data.

Nanoparticle Vaccines

Nanoparticle vaccines use very small particles to carry vaccine proteins to the body. They can copy the structures of pathogens, which boosts the immune system. Nano vaccines are made up of a chosen antigen attached to a nanomaterial and an adjuvant that makes the immune system react. Nanoparticles can have many antigen epitopes (shown by red and blue antigens) attached to their surface. The different iron oxide nanoparticles that are used in medicine right now have half-lives in the blood that range from 1 hour to 24 to 36 hours. However certain biodistribution and clearance parameters rely on the properties of the particles, like their shape, size, and surface features. COVID-19, HIV, Merkel Cell Polyomavirus, influenza A virus, and a lot of other vaccines are made with nanoparticles. Nanovaccines for antigen delivery were created to keep the specific antigen that was released from breaking down after it was given. Nano vaccines are useful because they naturally guard the antigen they deliver, which is very important. Even though the latest vaccine studies have shown promising results, there are still many problems that need to be fixed to make the cancer effects stronger and last longer. These problems include poor stability, weak immunogenicity, and strong toxicity.

Pros [17]**:**
- Enhanced immune response and durability.
- Potential for multivalent vaccines targeting multiple pathogens.

Cons [18]**:**
- Limited experience with these vaccines outside the COVID-19 context.
- Manufacturing and distribution challenges.

Conclusion

The world of vaccination has witnessed substantial progress, offering a wide array of vaccine types for diverse health challenges. From traditional live attenuated and inactivated vaccines to the innovative DNA, mRNA, and nanoparticle vaccines, each type presents unique strengths and limitations. The choice of vaccine type hinges on factors such as pathogen characteristics, target population, safety considerations, and logistical constraints. Continuous research and development promise to expand our arsenal against infectious diseases, providing hope for improved disease prevention and treatment in the future.

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