ISSN 2744-1636
Review Article

Bioengineering Studies
Vol. 5, No. 1, July 2024, pp.36-42
https://doi.org/10.37868/bes.v5i1.id318

Immunology and Vaccinology - a short review

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Received Jun. 30, 2024
Revised Jun. 15, 2024
Accepted Jun. 30, 2024

Abstract

Vaccines are used to stimulate an immune response to a specific infectious disease or pathogen. They contain an inactive or weakened pathogen, or its parts, causing our immune system to react and remember the encounter with its antigens. After vaccination, the immune system produces antibodies that destroy the pathogen while preventing the infection. Since the production of the first successful vaccine in 1796 until today, dozens of different types of vaccines have been produced. With the development of biotechnology, we have gone from empirically made vaccines to those that use only a small molecule of mRNA for the defense against pathogens. Nowadays, vaccines are not only used as protection, but also to treat diseases, such as cancer, addiction, or allergies. This review aims to inform a broad scientific audience about basic immunological concepts, more specifically, the immune system and its response, vaccines, and related challenges.

Keywords: Immunology, Vaccination, lymphocytes, T cells, pathogens

1. Introduction

Although the first successful vaccine was made more than two hundred years ago, vaccines are still considered one of the greatest discoveries in medicine today. With the discovery of antibiotics and improved sanitation, vaccines are the most effective weapon in the fight against microbes [1]. Vaccines contain an inactive pathogen or its parts, which causes our immune system to react and remember the encounter with the antigens of the pathogen. After vaccination, the immune system produces antibodies that destroy the pathogen and prevent infection [2]. Although there have been numerous attempts to produce vaccines before, the first successful vaccine was produced by the English physician Edward Jenner in 1796 [3]. He successfully cured a boy of cowpox. That is why the word vaccine is derived from 'Variolae vaccinae', which means 'pustules of the cow'. From that day until recently, vaccines were made exclusively empirically, which involved the injection of a dead pathogen or exposure to natural infection in order to acquire immunity. This type of vaccine was effective, didn’t require much knowledge about immunological responses, and saved millions of lives of people suffering from hepatitis, rubella, and chickenpox. However, soon vaccine failures for HIV, influenza, and other pathogens emerged [4]. Decades passed until a full understanding of the immune mechanisms of the body and how vaccines provide protective immunity was established. It soon became clear that treating some infections requires much more than injecting an inactive pathogen, and that the immune response to a vaccine is extremely complex. After the discovery that the immune system has different types of responses to protect against different pathogens and that understanding immunology is the key to producing an effective vaccine, different types of vaccines began to be created [5].

2. Understanding basic principles of immunology

Immunity is the body's ability to resist the pathogen [6]. Two types of immune systems exist: innate and adaptive. The innate immune system, also called non-specific, includes the first line of defense against pathogens: skin, mucous membranes, and immune cells and proteins. However, if the innate immune system fails to fight the pathogen, the adaptive or specific immune system takes over. The adaptive immune system directly targets the pathogen that caused the infection. The adaptive immune system reacts more slowly than the non-specific one, because it first needs to identify the pathogen to attack it. The adaptive immune system consists of T lymphocytes, B lymphocytes, and antibodies [7].

The immune response and its memory depend on T lymphocytes, a type of white blood cell. T lymphocytes contain specific receptors that can recognize antigens on pathogens, tumors, or any other cells that can threaten the homeostasis of our organism. The function of T lymphocytes depends on their type, of which there are many. For example, killer T cells, or CD8+ T cells, secrete cytokines and directly kill the infected cells [8]. On the other hand, CD4+ T cells, also known as helper T cells, help activate B cells and killer T cells. CD4+ cells are thought to be the most important type of cells in our immune system because they are needed for any type of immune response [9]. Lastly, T regulatory or T suppressor cells have the role to suppress the immune response and to maintain the homeostasis of our organism [10].

The main role of B lymphocytes is to produce antibodies that are necessary to destroy pathogens. These cells have the ability to recognize many types of antigens found on invasive microbes, and in response, B cells differentiate into antibody-secreting plasma cells, which synthesize antibodies [11].

Human antibodies are classified into five isotypes, each with different structures and functions. The IgG antibody is considered the major antibody and can be found in the human serum, on the surface of mature B cells. Its main role is to neutralize toxins, bacteria, and viruses. The IgG antibody has the ability to pass through the placenta, so the mother's IgG protects the fetus as well [12]. IgM pentamer is first produced by B cells during the defense of the organism against pathogens and therefore plays a key role in the initial immune system defense [13]. Immunoglobulin A is an antibody that plays a role in the immune function of mucous membranes, respiratory, and gastrointestinal tracts. It is the second most abundant immunoglobulin type found in the human body and plays a very important role in defense against antigens. It is present in breast milk and thus protects newborns from infections [14]. Immunoglobulin D has a role in the induction of antibody production, along with the prevention of respiratory tract infection [15]. On the other hand, IgE is believed to be related to allergies such as pollinosis [16].

3. Classification of vaccines

3.1. Live attenuated vaccines

Live attenuated vaccines have been developed by empirical clinical studies and are considered the first and most effective types of vaccines in human and animal history. For reference, the last case of Rinderpest, a contagious viral disease affecting cows, sheep, pigs, and goats, occurred in Kenya in 2001. This successful case makes the Rinderpest vaccine the most effective live attenuated vaccine to date [17]. Live attenuated vaccines contain a version of the living but weakened pathogenic microbe. This is achieved in a way that the pathogen passes through a foreign host many times and introduces mutations into the new host. Tissue cultures or oocytes are usually used as hosts. After one such batch, the mutated pathogen is significantly different and weaker than the original, strong enough to trigger an immune response but not to cause infection [18]. This type of vaccine requires very little understanding of viral pathogenesis and modification, but there is a risk of reversion to virulence. Nowadays, this type of vaccine is regularly used to provide protection against rotavirus, chickenpox, and influenza.

3.2. Inactivated vaccines

Another type of empirically made vaccines is inactivated vaccines. They are similar to attenuated, except that the inactivation of the virus in these vaccines is caused by chemical or heat reactions. Inactivated vaccines do not provide complete protection against pathogens, so they are administered in several doses. Today, inactivated vaccines are used to protect against hepatitis A and poliovirus. Given that inactivated vaccines have been used for decades, this platform has been employed in COVID-19 vaccines when the epidemic took over the world. Moreover, this type of vaccine has been shown to be particularly effective in providing protection against the delta strain of the coronavirus, when all required booster doses have been taken [19]. One of the leading advantages of these vaccines is the storage temperature, which starts from 2 to 8 °C, which allows less well-equipped health institutions to use them. However, inactivated vaccines are associated with concerns of antibody-dependent enhancement (ADE). ADE occurs when antibodies recognize and bind to a pathogen, but they are powerless to prevent infection. What's more, these antibodies allow the pathogen to spread throughout our body. There is concern that this type of vaccine can lead to antibody-dependent enhancement, especially when we talk about new variants of the constantly mutating COVID-19 virus [20].

3.3. Subunit vaccines

Subunit vaccines contain only parts of the pathogen, usually antigens or glycoproteins that have the ability to cause a reaction of the host's immune system. The advantage of these vaccines is that they contain only the essential antigens of the microbe, which are enough to activate our defense mechanism without having many side effects. Nowadays, subunit vaccines are very effective in protecting against malaria, human cytomegalovirus, the novel severe acute respiratory syndrome coronavirus 2, and many other infectious diseases [21].

Nevertheless, there are certain drawbacks that these vaccines possess. It is known that all organisms tend to change and mutate over time. And so, with pathogens, there is a risk of mutation and reversion of virulence, which will then cause disease. Furthermore, these vaccines are not suitable for people with weakened immune systems, pregnant women, patients suffering from HIV, and those receiving chemotherapy, because of the immunological reactions they could cause [22]. This led to the need for a different, modern approach to vaccine development.

3.4. DNA vaccines

The coronavirus pandemic has significantly contributed to the development of new technology and new approaches to vaccine production. With the realization that COVID-19 is mutating very quickly and that new strains are constantly emerging, the need for an effective vaccine that can keep up with this trend has never been greater. Traditional vaccines contributed to protection against this virus; however, with these vaccines, it was very difficult to keep up with the constant new strains of the virus. Thus, in 2021, COVID-19 vaccines were developed using new DNA and mRNA technology.

DNA vaccines are based on the injection of a bacterial plasmid containing the DNA sequence encoding the targeted antigens. This modern approach has many advantages compared to the traditional type of vaccine, the biggest advantage being that it stimulates the production of B and T cells. Also, it does not contain any form of virus, so no infection will occur, but the immune system will respond and produce desired antibodies. They are also known as third-generation vaccines, which are also used for the protection of animals against pathogens. Another advantage of DNA vaccines is that they provide long-term persistence of immunogen after the vaccination. On the other hand, there are certain risks that the injected DNA will disrupt the function of genes that control cell growth, which can lead to major diseases. Until recently, DNA vaccines were only approved for veterinary use. However, in 2021, authorities approved the first DNA vaccine for humans and children, called ZyCoV-D. This vaccine was developed in India and serves to protect against COVID-19 [23].

3.5. mRNA vaccines

mRNA technology relies on introducing a piece of mRNA that corresponds to a viral protein. That protein is usually found on the viral outer membrane. The advantage is that the person who receives this vaccine will not be exposed to the virus in any way, nor will they be able to get infected by the vaccine, which can be the case with attenuated or inactivated vaccines. Once the targeted mRNA reaches the body, cells will produce the viral protein, which will stimulate the immune system to produce antibodies. Once produced, the antibodies remain in the body and are ready to defend the body against the real virus if an infection occurs [24]. With the use of these vaccines, a significant drop in the number of coronavirus patients was observed. It has already been proven that mRNA vaccines are more effective than inactivated vaccines, even though it provides lower level of safety. Another advantage of this type of vaccine is that the production process is very simple and fast. The disadvantage is that the mRNA molecule is unstable and easily degraded, and the effectiveness of these vaccines is weaker than DNA based vaccines [25]. The COVID-19 mRNA vaccine is currently the only approved vaccine of its kind; however, mRNA vaccines against influenza, Zika virus, HIV, and cytomegalovirus are currently being researched. Lastly, it is important to note that these vaccines are given in several doses, because the number of antibodies decreases after several months [26].

3.6. Viral vector vaccines

A viral vector vaccine is another modern approach in vaccine construction. This type of vaccine uses a viral vector in order to deliver genetic material (DNA) to the host, which encodes key antigens of the pathogen. That DNA is then transcribed by the cells as mRNA, coding for a desired protein or antigen, triggering an immune response. The most commonly used viral vectors are adenovirus, influenza, and poxvirus. This type of vaccine was used before the pandemic to protect against the Zika virus, malaria, and Ebola. However, with the advent of the pandemic, greater focus was placed on this technology, and the process of viral vector research was accelerated [27].

It is important to note that there are other types of vaccines, such as RNA vaccines, synthetic peptide vaccines, recombinant protein expression vaccines, toxoid, and many others [28].

Table 1. Advantages and disadvantages of different types of vaccines [22].

Type	Advantages	Disadvantages
Live attenuated vaccine	Strong immune response, similar to natural infection	Risk of infection, not suitable for immunocompromised patients
Inactivated vaccine	Strong immune response, safer than live attenuated vaccine	Not suitable for immunocompromised patients, risk of AED
Subunit vaccine	Safe, highly tolerated, and cannot cause infection	Low immunogenicity
DNA vaccine	Safe, long-term persistence of immunogen	Risk of mutations
mRNA vaccine	Safe, highly effective, fast production	Weaker than a DNA vaccine, mRNA can be unstable

4. Future perspectives

4.1. Vaccines for cancer treatment

The coronavirus pandemic significantly accelerated the process of creating new, more modern types of vaccines, and contributed to the fact that today vaccines are used for many different purposes, and not only for the protection against microbes. For example, cancer vaccines are a revolutionary discovery in the field of cancer treatment. They aim to enhance the activation of anti-tumor immune response. For example, prophylactic cancer vaccines were initially made to prevent the development of tumors, and they proved to be very successful in defending the body against HPV and hepatitis B viruses, also known as cancer-causing viruses [29]. There are currently four different types of cancer vaccines approved, one of which is Bacillus Calmette-Guérin (BCG). The Bacillus Calmette-Guérin vaccine was originally developed to protect against tuberculosis, but it has another use. It contains weakened bacteria to stimulate antibody production and improve the immune response. This vaccine is approved for the treatment of patients with early-stage bladder cancer [30]. Cancer vaccines are much more difficult to produce than regular ones, because the tumor itself is a very aggressive and complicated disease. Patients suffering from tumors already have a weakened immune system, and it is very complicated to design an effective vaccine system that will not further endanger their health. However, vaccines that are already approved to treat tumors are showing good results and giving patients hope. With that, it is expected that we will soon be using vaccines to treat almost every type of cancer.

4.2. Vaccines against addiction

Vaccines have another important application, which is to combat drug abuse. The first such vaccine was produced in 1970 and had the purpose of suppressing the use of morphine, vaccines against cocaine, methamphetamine, nicotine, and other opiates appeared. Although the first results of vaccines against nicotine and cocaine were promising, from 1970 until today, these vaccines have not lived up to their full potential due to difficulties in targeting antigens and dosing therapy. There were many successes in animal studies; however, only one vaccine for human use reached Phase III trials, called NicVax, and it was proven unsuccessful. Another challenge is that people who suffer from addiction most often do not have access to adequate health care and therefore will not have access to these vaccines [31]. Given that addiction is a serious problem worldwide, it is expected that scientists with current knowledge and a better understanding of the immune system will soon produce a vaccine that will not have such limitations, which will be a revolutionary breakthrough [32] [33].

5. Conclusion

From 1796 until today, the vaccine represents one of the greatest breakthroughs in human history. Through immunization, many diseases have been eradicated, and millions of lives have been saved. Vaccination has always been important, and vaccines have been developed and improved with the understanding of immunology and the development of biotechnology. The greatest focus on immunization was placed during the coronavirus pandemic, which contributed to the extremely rapid development of vaccinology. In addition to traditional live attenuated, inactivated, and subunit vaccines, new approaches have been developed in the construction of vaccines that use mRNA, viral vectors, DNA, and so on. Biotechnology has developed so much that vaccines are now not only a means of fighting infections, but also other diseases, such as cancer, addiction, or allergies. From this review, it can be concluded that the perfect vaccine that does not carry any risks has not yet been created. However, it is important to emphasize that with the constant mutation of pathogens and the emergence of new diseases, the process of creating new vaccines will always be ongoing. Therefore, a lot can be expected from this science in the future.

Declaration of competing Interest

The authors declare that they have no known financial or non-financial competing interests in any material discussed in this paper.

Funding information

No funding was received from any financial organization to conduct this research.

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