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Chapter

Vaccine Types

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Abstract

There are several different types of vaccines. Each type is designed to teach your immune system how to fight off certain kinds of germs and the serious diseases they cause. There are four main types of vaccines: live attenuated vaccines; inactivated vaccines; subunit, recombinant, polysaccharide, and conjugate vaccines; and toxoid vaccines.

Keywords: vaccine, type, attenuated, inactivated, recombinant

1. Introduction

Vaccines are biologics that provide active adaptive immunity against specific diseases. Vaccines usually contain drugs that resemble the microorganisms responsible for the disease and are often made from one of the killed or attenuated microorganisms, their toxins, or their surface proteins, introduced by mouth, by injection, or by nasal spray to stimulate the immune system in us and recognize the foreign agents and destroy them.

There are many success stories in vaccine. The first vaccine, against smallpox, a disease that had killed millions of people over the centuries by British physician Edward Jenner in 1796 [1], was derived from the benign cowpox virus, which provided immunity to small pox. In 1980, following an historic global campaign of surveillance and vaccination, the World Health Assembly declared smallpox eradicated. In the nineteenth and twentieth centuries, scientists following Jenner's model developed new vaccines to fight numerous deadly diseases, including polio, whooping cough, measles, tetanus, yellow fever, typhus, rubella mumps, varicella, and hepatitis B and many others [2]. Rabies was the first virus attenuated in a lab to create a vaccine for humans.

The vaccine exposes humans to very small and safe amounts of attenuated or killed viruses and bacteria. When you are exposed to it in later life, the immune system will learn to recognize and attack infections. So you will not get sick, or you may be infected lightly. During the process of immunity development, the body produces antibodies against specific microorganisms and creates defense. The next time the person encounters that microorganism, the antibody prevents him from causing disease or alleviates the severity of the disease, regardless of the way that a vaccine is made.

Vaccines are the most cost-effective healthcare interventions known to prevent death and disease. A dollar spent on a childhood vaccination not only helps save a life but greatly reduces spending on future healthcare. According to a new study from the University of North Carolina at Chapel Hill, vaccination efforts made in the world's poorest countries since 2001 will have prevented 20 million deaths and

saved $350 billion in healthcare costs by 2020 [3]. There are still numerous diseases causing globally significant morbidity and mortality, for which no vaccines are available. Millions of people worldwide die of malaria, tuberculosis, and AIDS every year, diseases without effective vaccines. This chapter describes the vaccine types now in use and that may lead to the vaccines of the future.

2. Different types of vaccines

There are several different types of vaccines. Each type is designed to boost your immune system and prevent serious, life-threatening diseases. Four types of vaccines are currently available:

- live attenuated vaccines;
- inactivated vaccines;
- subunit, recombinant, polysaccharide, and conjugate vaccines; and
- toxoid vaccines.

2.1 Live attenuated vaccines

Live attenuated vaccines contain a version of the living virus that has been weakened so that it does not cause serious disease in people with healthy immune systems. Live attenuated vaccines can be made in several different ways. The most common methods involve passing the disease-causing virus through a series of cell cultures or animal embryos (typically chick embryos). Viruses are often attenuated by growing them in cells that they do not normally grow in for many generations. With each passage, the virus becomes better at replicating in new cells but loses its ability to replicate in human cells. Eventually, the attenuated virus will be less able to live in human cells and can be used in a vaccine. This method selects mutants that are more suitable for growth under abnormal culture conditions and is therefore less suitable for growth in natural hosts. Therefore, when attenuated viruses are given to a human, they are not able to replicate enough to cause illness like they would naturally but will still provoke an immune response that can protect against future infection. Albert Sabin's oral polio vaccine and measles, rubella, mumps, and varicella vaccines are all achieved by in vitro cell culture passage selection clones. The poliovirus used in the Sabin vaccine is attenuated by the growth of monkey kidney epithelial cells. The measles vaccine contains a strain of rubella virus that grows in duck embryo cells and later grows in human cell lines [4–8]. Another live vaccine that has so far only been used in the military to prevent epidemic pneumonia includes adenoviruses 4 and 7 grown in human diploid cell lines and orally administered for replication in the intestine [9]. Other live vaccines that are attenuated in cell culture passages are attenuated monovalent rotavirus vaccines in Vero cells [10] and Japanese encephalitis virus strain SA14-14-2 [11]. Some viral vaccines are grown in chicken eggs; live attenuated influenza vaccine and yellow fever vaccines are currently produced in embryonated hen's eggs, a method developed in the late 1930s [12, 13].

Live attenuated vaccines have advantages and disadvantages. Live attenuated vaccines are ideal for teaching the immune system against specific viruses because they are closest to natural infections. They often require only a single immunization, eliminating the need for repeated boosters. And these vaccines are relatively easy to create for certain viruses.

The Sabine polio vaccine consists of three attenuated poliovirus strains that are orally administered to children in sugar cube or sugar liquid. The attenuated virus colonizes the gut and produces protective immunity against all three virulent poliovirus strains. Unlike most other attenuated vaccines that require a single immunization dose, the Sabin polio vaccine requires a booster because the three attenuated polioviruses in the vaccine interfere with each other's replication in the gut.

The main disadvantage of attenuated vaccines is the possibility they will revert to a virulent form and cause disease. These vaccines cannot be administered to people with weakened immune systems due to cancer, HIV, or other immune system depressing diseases. Attenuated vaccines also may be associated with complications similar to those seen in the natural disease. Live attenuated vaccines usually have to be refrigerated and protected from light. It can be difficult to ship these vaccines overseas and use them in places where there is lack of refrigeration. This technique does not work well for bacteria; therefore there are few live bacterial vaccines. The virus is very simple, but for bacteria, which have thousands of gene, is at least a hundred times larger than a typical virus. This makes bacteria more difficult to control and manipulate than viruses. Currently, scientists are trying to remove key genes from certain bacteria in order to create a weakened version for vaccines.

Immunization using this strategy are [14]:

Viral:

- MMR vaccine;
- *Rotavirus* vaccine;
- oral polio vaccine (not used in the USA);
- influenza vaccine (nasal spray) FluMist;
- varicella (chickenpox) vaccine;
- shingles vaccine;
- yellow fever vaccine;
- adenovirus oral vaccine (military); and
- *Vaccinia* vaccine.

2.2 Inactivated vaccines

Another common method of vaccine production is inactivation of the pathogen by heat or by chemical treatment. This destroys the pathogen's ability to replicate but keeps it "intact" so that the immune system can still recognize it. Maintaining the epitope structure on the epitope antigen during inactivation is critical. Heat inactivation is generally unsatisfactory because it results in extensive denaturation of the protein; therefore, any epitope that is dependent on higher levels of protein structure may change significantly. Chemical inactivation with formaldehyde or formalin has been successful. The Salk polio vaccine is produced by formaldehyde inactivation.

Because killed or inactivated pathogens cannot replicate at all, they cannot revert to a more virulent form capable of causing disease (as discussed above with live attenuated vaccines). Attenuated vaccines generally require only one dose to induce long-lasting immunity. However, inactivated vaccine tends to provide a

shorter length of protection than live vaccines and is more likely to require boosters to create long-term immunity.

A vaccine consisting of orally administered killed cholera bacteria with or without the B subunit of cholera toxin has been developed [15]. Formalin-inactivated whole-cell pertussis vaccine was tested by Madsen [16], and later it was shown to be relatively successful in controlling severe disease [17]. In 1923, Glenny and Hopkins reduced the toxicity of diphtheria toxin by formalin treatment [18]. Ramon has improved this finding and has shown that it is possible to inactivate the toxicity of these molecules while retaining their ability to induce toxin-neutralizing antibodies [19]. In the twentieth century, chemical inactivation was also applied to viruses. Influenza vaccine was the first successful inactivated virus vaccine [20].

Inactivated whole bio vaccines still present certain risks, even if they contain killed pathogens. When formaldehyde failed to kill all viruses in both vaccine batches, serious complications of the first Salk vaccines occurred, which led to a high proportion of polio (poliomyelitis).

Inactivated vaccines are used to protect against:

- hepatitis A;
- flu (shot only);
- polio (shot only); and
- rabies.

2.3 Subunit, recombinant, polysaccharide, and conjugate vaccines

The first vaccine, the smallpox vaccine, consists of live attenuated viruses, but it does not cause disease in human hosts. Many of the vaccines used today, including measles vaccines, yellow fever vaccine, and some influenza vaccines, use live attenuated viruses. Others use inactivated forms of toxins made from killed form of virus, debris of bacteria, or bacteria. The killed virus, bacterial debris, and inactivated toxins will not cause disease but will still cause immune reactions and prevent future infections. However, new techniques are also being developed to make different types of vaccines.

Subunit, recombinant, polysaccharide, and conjugate vaccines are biosynthetic vaccines. Biosynthetic vaccines contain man-made substances that are very similar to pieces of the virus or bacteria. The hepatitis B vaccine is an example.

Since these vaccines use only specific pieces of the germ, they show a very strong immune response, which targets the main part of the germ. It can also be used by almost everyone who needs them, including people with weakened immune system and long-term health problems. Vaccines consisting of specific purified molecules derived from pathogens can avoid some of the risks associated with attenuated or killed organism vaccines.

One limitation of these vaccines is that you may need booster shots to get ongoing protection against diseases.

Subunit vaccines use only a subset of target pathogens to stimulate the immune system's response. This can be done by isolating a specific protein from the pathogen and presenting it separately as an antigen. Acellular pertussis vaccines and influenza vaccines (injected forms) are examples of subunit vaccines.

Another subunit vaccine can be created by genetic engineering. The gene encoding the vaccine protein is inserted into another virus or inserted into a cultured production cell. Vaccine proteins are also produced when the vector virus

is propagated. The result of this approach is a recombinant vaccine: the immune system will recognize the expressed protein and provide future protection against the target virus. Many genes encoding surface antigens from viral, bacterial, and protozoal pathogens have been successfully cloned into bacterial, yeast, insect, or mammalian expression systems, and the expressed antigens are used for vaccine development. A hepatitis B vaccine that is approved for use in humans is a recombinant vaccine. The vaccine was developed by cloning the hepatitis B virus surface antigen (HBsAg) gene and expressing it in yeast cells. Recombinant yeast cells proliferate in large fermenters, and HBsAg accumulates in cells. At the end of the fermentation, recombinant HBsAg are harvested by disrupting yeast cells, which is then purified by biochemical techniques. This recombinant hepatitis B vaccine has been shown to induce the production of protective antibodies [21, 22].

Human papillomavirus (HPV) vaccine is another vaccine made using genetic engineering. Two types of HPV vaccine are available, Gardasil (marketed by Merck and protecting against types 6, 11, 16, and 18 of the human papillomavirus) and Cervarix (marketed by GlaxoSmithKline and protecting against types 16 and 18 only). Both are made in the same way: for each strain, a single viral protein was isolated. When these proteins are expressed, viruslike particles (VLPs) are produced. These VLPs contain no genetic material that causes disease but promote immune responses and protect future HPV infection.

Recombinant vector vaccines use attenuated viruses (or bacterial strains) as vectors. A gene encoding a major antigen of a particularly virulent pathogen can be introduced into an attenuated virus or bacterium. The attenuated organism acts as a vector that replicates and expresses the gene product of the pathogen in the host.

Baculovirus which is a virus that infects only insects can be used as a vector, and genes for specific immunogenic surface proteins of influenza virus can be inserted. Once the modified virus is introduced into humans, the immunogen is expressed and displayed, producing an immune response against the immunogen and producing an immune response to the immunogen from which it is derived. In addition to insect viruses, human adenoviruses have been identified as potential carriers for recombinant vaccines, particularly against diseases such as AIDS. *Vaccinia virus*, the attenuated vaccine used to eradicate smallpox, was the first used in live recombinant vaccine approaches [23]. This large, complex virus, with a genome of about 200 genes, can be designed to carry dozens of foreign genes without compromising their ability to infect host cells and replicate. Experimental recombinant vaccinia strains have been designed to provide protection against influenza, rabies, and hepatitis B and other diseases.

DNA vaccines consist of plasmid DNA encoding antigenic proteins which are injected directly into the muscle of the recipient. The DNA itself inserts into the individual's cells, which then produce the antigen from the infectious agent. DNA vaccines have advantages over many existing vaccines. For example, the encoded protein is a native form of the host and has no denaturation or alteration. Therefore, the immune response is identical to the antigen expressed by the pathogen. The handling and storage of plasmid DNA do not require refrigeration, a feature that greatly reduces the cost and complexity of delivery. At present, there are human trials underway with several different DNA vaccines, including those for malaria, AIDS, influenza, and herpesvirus. Researchers hope that DNA vaccines can produce immunity against parasitic diseases such as malaria; however, there is currently no human vaccine in use for fighting parasites [24].

Conjugate vaccines are somewhat similar to recombinant vaccines: they are prepared using a combination of two different components. The conjugate vaccine was prepared using fragments from the coats of bacteria. These coatings are chemically linked to a carrier protein which is used as a vaccine. Conjugate vaccines are used to produce a more powerful co-immune response: in general, the presented

"fragments" of the bacteria do not themselves produce a strong immune response, while the carrier protein produces a strong immune response. This fragment of bacterium does not cause disease, but when combined with carrier proteins, it can produce immunity against future infections. The vaccines currently in use for children against pneumococcal bacterial infections are made using this technique.

These vaccines are used to protect against:

- *Haemophilus influenzae* type b (Hib) disease;
- hepatitis B;
- human papillomavirus (HPV);
- whooping cough (part of the DTaP combined vaccine);
- pneumococcal disease;
- meningococcal disease; and
- shingles.

2.4 Toxoid vaccines

Toxoid vaccines are made from selected toxins that have been sufficiently attenuated and are able to induce a humoral immune response. These toxins produce many of the symptoms of the disease. For example, diphtheria and tetanus vaccines can be prepared by purifying bacterial toxins and then inactivating toxin with formaldehyde to form a toxoid. Inoculating with a toxoid induces an anti-toxoid antibody that is also capable of binding toxins and neutralizing their effects.

Toxoid vaccines tend not to have a duration of immunity comparable to attenuated viral vaccines; therefore, toxid vaccines, like some other types of vaccines, may need booster shots to get ongoing protection against diseases. Revaccination (booster) may be required multiple times in a single year depending on individual patient risk factors.

Toxoid vaccines are used to protect against:

- diphtheria; and
- tetanus.

3. Summary

There are still the needs for vaccines against other diseases. Millions of people worldwide die of malaria, tuberculosis, and AIDS every year, among which there are no effective disease vaccine. The road to successful development of vaccines that can be approved for human use, reasonably manufactured cost, and effective delivery to high-risk groups is expensive, long, and tedious.

Researchers continue to develop new vaccine types and improve current approaches.

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Conflict of interest

We have no conflict of interest.

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