Different Vaccine Types and Advancements

W. Jean Dodds, DVM | Hemopet | 11561 Salinaz Avenue Garden Grove, California | 714.891.2022

Vaccine innovations are rapidly expanding to develop new, more effective, alternative or safer vaccines against a wide variety of diseases in people and animals. While vaccines carry both health benefits and some health risks, we decided to step back and provide you with a basic glossary of the types of vaccines currently available, vaccination variables, words commonly associated with vaccines, and what vaccines are on the horizon.

Vaccines for Diseases – Available and in Development

Vaccine development for many different diseases is ongoing.

- Most vaccines used today are to protect against viral and bacterial infections.
- Autoimmune and cancer vaccines for humans are in development and a few are in early phase clinical trials. A vaccine for canine melanoma cancer is on the market, but this vaccine is given after a dog is diagnosed with the disease and is refractory to routine therapies.
- Allergen-specific immunotherapy – commonly referred to as “allergy shots”, is a form of vaccination against specific allergies.
- Vaccines against fungal infections are not on the market, but are in development, although a ringworm vaccine for dogs was marketed and withdrawn some years ago.

Administration Methods

How a vaccine is administered is very important to make sure it is “taken up” by the body and causes minimal side effects or injection site reactions.

- Injection
- Orally
- Aerosol (intranasal)
- Skin patch application (in development)
- Gene gun (biolistic particle delivery system)

Age and Timing of Vaccinations

The age of the human or animal is critical to successful and safe immunization when a vaccine is administered. For instance, the majority of dogs should receive distemper and parvovirus vaccines between nine and ten weeks of age. If these vaccines are given too young, they will conflict with (be partially neutralized by) the residual maternal antibodies conveyed against these diseases through colostrum, which is found in breast milk during the first 36 hours of life. Eventually, colostrum–derived antibodies gradually wane from birth over about three months and most are gone by the age of 14-16 weeks. Conversely, the period of highest vulnerability to infectious diseases is between 10-14 weeks of age. So, puppies should receive at least one dose of the distemper and parvovirus bivalent (preferred) or a multivalent vaccine between 9 and 10 weeks of age, even though it will only partially immunize them. Then, boosters between 14 and 15 weeks and a third parvovirus only vaccination at 18 weeks of age, to add extra protection against the current highly virulent canine parvovirus strains.

Terms to Know When Reading This Article

- Adjuvants – substances added to certain vaccines to enhance and prolong their effectiveness.
- Antigen – foreign substance or toxin that induces an immune response in the body.

- Epitopes – the specific parts of the antigen to which antibodies or T-cells bind themselves.
- Immunogenicity – the ability to induce the desired humoral (B-cell) and/or cell-mediated (T-cell) response to generate immunity.
- Peptide – a compound consisting of two or more amino acids linked in a chain.
- Plasmids – small DNA molecules within cells that are physically separated from chromosomal DNA and can replicate independently.

Live, Attenuated/Modified Live Vaccines

Attempts at vaccination have been around for centuries, but the type of vaccine that has been around the longest is a live, attenuated product that is also known as a modified live vaccine (MLV). They use a modified (attenuated), but weakened, form of the live microorganism. When the virus is given, it multiplies many-fold and stimulates the immune system's production of antibodies, creating an immune response that protects the body against future exposure to the disease. When given appropriately, these vaccines are important and essential to protect the health and longevity of people and animals. However, side effects can occur such as an autoimmune diseases, inflammation, tissue damage, seizures, cancers, reactions to vaccine excipients, and even tumors at the injection site.

Examples of the common so-called "core" modified live vaccines for dogs are for the viruses canine distemper, adenovirus-2 (hepatitis), parvovirus and parainfluenza; also commonly given are vaccines for the bacterium *Bordetella* (oral, intranasal, or injectable). [Note: This author prefers the oral vaccine which releases interferon of the vaccinated dog which then cross-protects against the other canine upper respiratory viruses. Intranasal Bordetella can spray vaccine virus around the face and those nearby and he injectable vaccines does not induce release of interferon and its cross-protection.]

Killed Vaccines

Killed vaccines use an inactivated or "dead" form of the virus (previously live microorganisms that have been killed with chemicals or heat), along with an adjuvant. Note that adjuvants are implicated in the ASIA -syndrome (autoimmune inflammatory syndrome induced by adjuvants) in people and animals. Mercury and aluminum, other metals as well as the many excipients used in vaccines have been implicated.

Killed adjuvanted vaccines for dogs include all rabies vaccines, canine leptospirosis, Lyme, canine influenza, and the injectable Bordetella.

What about cats? Cats have a wider variety of options for vaccines in comparison to dogs. For example, a non-adjuvanted feline rabies vaccine is available. Most vaccines for cats come in MLV (*not* recommended for pregnant queens or very young kittens), combination killed and intranasal versions.

Toxoid

Toxoid vaccines are best explained using an example: tetanus. A tetanus vaccine does not protect you from the bacteria *Clostridium tetani*, but protects you from the toxic substance (poison) the bacteria can cause. In essence, the vaccine creates immunity to the parts of the bacteria that cause lockjaw instead of the bacteria itself.

Recombinant Vaccines

It is best to think of "recombinant" as simply a descriptor of how a vaccine is manufactured. It is the complex process of recombining. So, while you might read "recombinant vaccines", the phrase refers more to the vaccine technology rather than the vaccine.

Recombinant vaccines rely on the capacity of one or more antigens to induce immunity against a pathogen, when administered with adjuvants or when expressed by harmless bacterial/viral vectors or plasmids.

One type of recombinant vaccine is recombinant protein vaccines (also known as recombinant subunit vaccines), which rely on recombinant DNA technology. However, these are not considered DNA vaccines. This technique involves inserting the DNA encoding antigen – such as a bacterial or viral surface protein – that will then stimulate an immune response when inserted into bacterial or mammalian cells. The best known vaccines that use this recombinant DNA technology are against human hepatitis B. However, it is not considered a DNA vaccine.

Recombinant vector vaccines (platform-based vaccines) use an attenuated virus or bacterium to introduce microbial DNA to the cells of the body. "Vector" refers to the virus or bacterium used as the carrier. Again, these are not DNA vaccines.

Recombinant vector and subunit veterinary vaccines have recently been available for pets for use against canine distemper and Lyme disease, respectively.

An oral rabies virus vaccine exists for raccoons and coyotes. It is only sold to government agencies that are conducting rabies control programs.

Subunit

Oftentimes when researchers write "subunit vaccine", they are referring to protein-based subunit vaccines, as mentioned above. To be clear, other subunit vaccines also exist: polysaccharides (sugars), conjugates, and detoxified toxins.

Also to clarify, only recombinant protein-based vaccines have been developed, but not all protein-based vaccines are recombinant. However, research suggests that recombinant conjugate vaccines using recombinant DNA technology may soon be available.

So, what are subunit vaccines? Instead of the entire microbe used like in MLV or killed vaccines, subunit vaccines only have the antigens that best stimulate the immune system against disease. In some cases, these vaccines use epitopes. Because subunit vaccines contain only the essential antigens and not all the other molecules that make up the microbe, the chances of adverse reactions to the vaccine are generally lower.

Of course, this precision to develop a subunit vaccine comes at a cost and can be tricky. Antigenic properties of the various potential subunits of a pathogen must be examined in detail to determine which particular combinations will produce an effective immune response within the correct pathway.

Regarding the various categories of subunit vaccines, polysaccharides protect some bacteria when they invade the body. So, the logical conclusion would be a polysaccharide subunit vaccine. Unfortunately,

polysaccharide vaccines against these bacteria tend not to be effective in infants and young children, and induce only short-term immunity. To circumvent this issue, conjugate subunit vaccines were developed, which bind the polysaccharide to a carrier protein that can induce longer term protection.

Synthetic Vaccines

The protein-based subunit recombinant DNA hepatitis B vaccines, mentioned earlier in this article, are synthetically prepared so they do not contain blood products. It is impossible to get hepatitis B from the vaccine. But… While subunit vaccines are considered safer than MLV vaccines, they are still not perfectly safe. They can cause side effects and experience production difficulties.

As an alternative, researchers these days are making the case for more experimentation into peptide-based synthetic vaccines. They state that peptide-based vaccines will allow focusing solely on relevant epitopes, avoiding those that lead to nonprotective responses, immune evasion, or unwanted side effects like autoimmunity. Additionally, these vaccines are typically water-soluble, stable under simple storage conditions, and can be freeze-dried.

Why haven't peptide-based synthetic vaccines been developed already? Because, technologies did not exist before to overcome the numerous difficulties associated with these vaccines. A couple of significant recent developments are solid-phase peptide synthesis and microwave techniques. These would allow peptide production to become simple, easily reproducible, fast and cost-effective.

Peptide-based vaccines also have low immunogenicity. To produce the desired immune response, scientists would have to add a relatively toxic adjuvant. However, improved and safer experimental adjuvants with proven efficacy in the induction of immune responses against peptides are being explored.

DNA Vaccines

Research into DNA vaccines is exploding. In fact, defining "DNA vaccine" is next to impossible. At this point, the simplest way to explain a DNA vaccine is one in which the DNA containing the genetic information to produce the antigen is introduced to the body. Then, the DNA provides the instructions to the body to produce the antigen.

We have read several research papers on the topic. We noticed that some DNA vaccines work and some do not. Overall, no one should be discouraged. Researchers definitely have a vision of what DNA vaccines could do to protect against infectious diseases, autoimmune diseases, allergies, and cancers.

Advantages of DNA Vaccines:

- Inexpensive
- Long-term persistence of immunogenicity
- Ease of development and production allow rapid response to epidemics and pandemics
- Immune response focused only on antigen of interest
- Stability of vaccine for storage and shipping
- More stable and easy to handle
- Induce protective humoral and cellular immune responses
- Heat stable

Disadvantages of DNA Vaccines:

- Limited to protein immunogens (not useful for non-protein based antigens such as polysaccharides). Certain vaccines, such as those for pneumococcal and meningococcal infections, use protective polysaccharide antigens
- Inducing antibody production against DNA
- May induce immunologic tolerance by antigens expressed inside the host body
- May have a relatively poor immunogenicity
- Atypical processing of bacterial and parasite proteins
- Insertion of foreign DNA into the host genome may cause the cell to undergo oxidative stress and free-radical production which becomes cancerous

RNA Vaccines

RNA vaccines are similar to DNA vaccines in that they tell the body to produce the antigen itself. RNA might not seem as exciting as DNA, but we have to remember the function of RNA. DNA produces RNA; and RNA then creates proteins.

One of the issues with DNA is that it has to first go through a transcription process. This process of transcribing DNA into RNA changes the information from a double-stranded into a single-stranded molecule, and all the DNA thymine bases into RNA uracil bases. So, if this process needs to occur, why not cut to the chase and develop RNA vaccines?

RNA vaccines also appear to be safer than DNA vaccines since they do not disrupt an original cell's natural DNA sequence.

Research appears to be focused on non-amplifying and self-amplifying messenger RNA (mRNA). A drawback with non-amplifying mRNA is that it only encodes the antigen of interest. So, research is also focusing on self-amplifying mRNA, which encodes both the antigen of interest and those proteins enabling RNA vaccine replication.

Does this all sound complicated biotechnology? You bet it is, and yet it represents the wave of the future for improved, targeted and safer vaccines.

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