The Future of Livestock Vaccines

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What is it?

A vaccine is a human-made substance used to trigger an immune response and the production of antibodies and other immune mediators. Antibodies are proteins, produced naturally when the body is exposed to disease-causing microbes, they help to eradicate infectious organisms. A vaccine causes production of antibodies before exposure to the microbe in order to provide a better chance of fighting the disease.

Vaccines have impacted public health greatly, allowing immunization programs in humans and livestock that have eradicated disease which once overwhelmed populations. Vaccination of livestock is an effective method of preventing infectious disease and is a key part of a complete herd/flock health management plan. It is also an important factor in protecting human health because livestock and humans are susceptible to and can spread several disease organisms. There are new technologies that will impact vaccine production, including the use of mRNA, now widely known as a result of the COVID-19 pandemic.

Types of livestock Vaccines:

Modified Live Vaccines

Live Attenuated

Must be attenuated (weakening the viral properties) so that the virulence can be replicated but not pathogenic, this requires intense studies to ensure there is stability. (Under-attenuated risks virulence, over-attenuated risks ineffectiveness)

Gene-Deleted

Using a molecular genetic technique to modify genes of an organism so that it stays irreversibly attenuated.

- First used against the Aujeszky disease herpesvirus in swine, the thymidine kinase gene was removed from the virus, thus it is able to infect neurons but cannot replicate and cause disease in the host.

Virus-vectored

These involve inserting the genes that encode protective antigens into an avirulent (without disease), vector organism. Essentially substituting the virulent genes from the vector and replacing them with genes that code for antigens from the pathogen.

- Well-suited for use against organisms that are difficult or dangerous to grow in a laboratory. Used for the West Nile virus in horses, Fowlpox virus and herpesvirus in poultry.

Non-Living Vaccines

Subunit

These contain fragments of protein and or polysaccharide from the pathogen. They are carefully studied to produce an immune response from an identified, isolated and pure critical protective antigen.

- Subunit vaccines typically require repeated doses and subsequent boosters to continue immune response

Antigens generated by Gene Cloning

This vaccine clones genes that code for protective antigens so that the DNA with the desired antigens can be inserted into the vector host. The vector is grown, harvested, purified and administered as a vaccine.

- This has been used for Lyme disease in dogs.

DNA Plasmid Vaccines

DNA encoding viral antigens are injected and inserted into bacterial plasmid, a circular DNA that acts as a vector. Once injected the vector is taken up by host cells and transcribed, mRNAs are translated to produce a vaccine protein. This results in development of neutralizing antibodies and cytotoxic T cells.

- Plasmid Vaccines have been used for avian influenza virus, bovine viral diarrhea virus, porcine herpesvirus. Ideally suited for organisms that are difficult to grow in cell culture. Induces production of viral endogenous antigens (antigens produced from within a cell normally).

Alphavirus Replicons

This RNA vaccine induces production of endogenous antigens, however, they are more stable than DNA plasmids and more efficient as they can enter through the cell cytoplasm. These can be self-replicating and generate large amounts of the endogenous antigen when they replicate.

- Alphavirus Replicons have been used for the Venezuelan equine encephalitis virus.

(Tizard, 2020)

Why it matters to the Ontario livestock industry:

The livestock sector in Ontario is a key driver of Ontario's economy, generating about $4 billion in value annually (Statistical Summary of Ontario Agriculture, 2016). The health of the herd and flock plays a huge role in the profitability of production but also in the environmental footprint and in food safety. Good health starts with biosecurity; however, disease will always be an issue for livestock producers. Treatment can be effective, although, there is rising concern regarding the use of antimicrobial products and the rise of antimicrobial resistance (AMR) (Refer to LRIC's Antimicrobial Use and Resistance White Paper for more information on this subject). Vaccines present less of a risk to the future of animal health than antibiotics and treatment medicine, with no AMR threat. Further, there is a growing understanding of the need to view livestock health as highly intertwined with health of humans and the environment. This concept is called One Health (Refer to LRIC's One Health White Paper for more information on this subject).

New technologies (e.g. mRNA, artificial intelligence) will have dramatic impact on the availability and effectiveness of vaccines available to producers. Artificial Intelligence (AI) has been used to accelerate drug discovery and identification of molecular determinants of microbes needed for vaccine development. In addition, new genomics, proteomics and transcriptomics techniques have allowed identification of potential proteins that can be utilised for development of vaccines (Sidik et al., 2016). Finally, CRISPR/Cas9 technology is a powerful system in regards to understanding molecular and cellular biology of disease-causing microbes and how hosts respond to microbes. Having a comprehensive understanding of host-microbe interactions will pave the way for development of novel and more efficacious vaccines that are cost-effective and easy to deploy. This can mean great things for the future of livestock vaccines (Sidik et al., 2016). The current COVID-19 pandemic has taught us many lessons, including the fact that the development, mass production and approval process of vaccines could be shortened from several years (or decades) to 8-9 months. This will have a significant and long-lasting impact on how livestock vaccines are produced and deployed in the future. It is now in the realm of possibility that a vaccine be developed and tested against an emerging pathogen of livestock and be deployed in the face of a global outbreak.

What can livestock farmers do?

First and foremost, producers should have a clear, documented and well implemented biosecurity plan. This should form a key part of a herd/flock health management plan, developed in consultation with a veterinarian. A vaccination program will complement the other elements of the herd/flock health management plan.

Ensure your herd/flock has the conditions (e.g temperature, air quality) and feed/water needed for optimal health. Vaccines are well proven to maintain livestock health but there are variables that can affect the efficacy. These include nutrition, biosecurity and environmental conditions (Vaccination of the Beef Herd, 2020). Despite wide adoption of vaccines by the livestock sector, there is still opportunity for wider use to protect livestock and reduce the use of antimicrobial products.

Consider vaccines that protect against several diseases (multivalent vaccines) as they are efficient at protecting the herd/flock. Vaccines are great at reducing mortality from common infections and in some cases, immunity conferred by vaccines are transferrable from mother to offspring.

Stay informed and educated on the various vaccines available, best done in consultation with your veterinarian.

Understand and adhere to vaccine-specifics including: timing, route of administration, dose, and expiration dates.

Keep up to date with what is going on in your area, what are other farms experiencing with their herds. Where possible, participate in disease surveillance networks.

When buying and selling livestock ensure that proper health and vaccination records are passed on with the animal.

History of livestock vaccines

- A French chemist, Louis Pasteur, developed a vaccine in 1879 to protect against chicken cholera, and in 1881 for anthrax of sheep and cattle.
- In 1884 The United States government created the Bureau of Animal Industry in the Department of Agriculture to create research and development with livestock and veterinary sciences.
- Prior to the development of mRNA vaccines, the common types of vaccines were live attenuated, inactivated, subunit, recombinant, polysaccharide, conjugate, and toxoid vaccines (Plotkin et al., 2013).
- The use of both live-attenuated or killed whole organism-based vaccines was very successful in limiting the spread of infectious diseases including classic swine fever, rinderpest, and equine infectious anemia (Patel & Heldens, 2009).
- mRNA vaccines were developed for treating cancer and were not commonly associated with infectious disease (Pardi et al., 2018).
- The global pandemic of 2019 brought mRNA technology to the minds of most people as it was used to produce mRNA vaccines for humans. These vaccines are easier and faster to produce compared to the traditional vaccine types (Pardi et al., 2018). The mRNA vaccines for COVID-19 have provided immunity levels that have not been seen using traditional types (Rachlin & Watson, 2017). mRNA vaccines are also less expensive as development and production uses readily available materials in a laboratory setting (Pardi et al., 2018).

Cultural Change

- Society is dealing with an exponential rate of change on many fronts, including genomics and artificial intelligence, both of which will impact vaccine development
- Prior to COVID-19, few people had heard of mRNA and now, many millions worldwide have been vaccinated as a result of that technology
- The mRNA technology made vaccine manufacturers rethink their traditional way to produce vaccines, still a lot of research is needed and mRNA might not be a solution for all kinds of diseases. To see its impact on livestock and poultry vaccines we will need to be patient to see if mRNA technology will arrive on the market
- Resulting from the pandemic, society is more attuned to the One Health concept and so vaccination of livestock will be seen as part of a larger health picture, one that includes humans and the environment

Research Gaps

- Develop efficacious vaccines for emerging or re-emerging livestock diseases, such as avian influenza
- Develop vaccines that can prevent or highly reduce "transmission" of disease-causing microbes
- Develop universal vaccines that can confer protection against a family of viruses (e.g. Coronaviruses or influenza viruses)

Innovation Gaps

- Develop new methods of administration
- Develop cost-effective vaccines that can be readily deployed to remote areas
- Develop vaccines that are resistant to environmental factors, e.g. are resistant to heat and do not require refrigeration
- Develop data capture and sharing systems to allow information on vaccination status to move with animals
- Develop global infrastructures and systems that address livestock vaccine inequity across the globe

For more information

1. Dr. Shayan Sharif, Professor and Associate Dean of Research and Graduate Studies for the Ontario Veterinary College, University of Guelph

Additional resources

- A guide to vaccinology: From basic principles to new developments – Nature reviews immunology by Andrew j. Pollard & Else M. Bijker

https://www.nature.com/articles/s41577-020-00479-7

- Vaccination 101: Set up your animals for success – Progressive Dairy by Jenna Hurty-Person

https://www.progressivedairy.com/topics/herd-health/vaccination-101-set-your-animals-up-for-success

- LRIC's Antimicrobial Use and Resistance in Livestock White Paper with contributing editor Jean Szkotnicki

https://livestockresearch.ca/uploads/cross_sectors/files/AMU-White-Paper-Final-Draft.pdf

- LRIC's One Health White Paper with contributing editor Dr. Heather Murphy

https://livestockresearch.ca/uploads/cross_sectors/files/Final-Draft-One-Health-White-Paper.pdf

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