PRINCIPLES OF VETERINARY VACCINOLOGY

VERSION 2

OUTLINES

JAMES A. ROTH, DVM, PhD, DACVM · GAYLE BROWN, DVM, PhD · KEVAN FLAMING, DVM, PhD

VETERINARY BIOLOGICS TRAINING PROGRAM

OIE

IICAB

the Center for Food Security & Public Health

IOWA STATE UNIVERSITY College of Veterinary Medicine

Principles of Veterinary Vaccinology

Principles of Veterinary Vaccinology

Introduction to Veterinary Vaccinology Topics

- Introduction
- Basis of Protective Immunity
- U.S. Veterinary Vaccine Regulations
  - Vaccine Labeling
- General Properties of Vaccine Types
  - Inactivated and Modified Live Vaccines
  - New Technology Vaccines
  - Adjuvants
- Reasons for Vaccine Failure
- Adverse Vaccine Reactions
- Duration of Immunity
- Vaccination in the Presence of Maternal Antibody
- Vaccination to Protect Mucosal Surfaces
  - Protection of the Respiratory Tract
  - Protection of the Enteric Tract
- Multifactorial Diseases
- Herd Immunity

Learning Objectives for Vaccinology

1. Describe the basic immunology for a protective immune response to an extracellular pathogen, an intravesicular pathogen, and an intracellular pathogen
2. Use your knowledge of disease pathogenesis to predict the protective immune mechanisms for a particular disease
3. Define titer and explain what information titer provides to the clinician and how the information can be used
4. List one- two advantages and disadvantages of MLV vaccines, inactivated vaccines, autogenous vaccines and new technology vaccines. Be able to justify why you might select one over the other in certain circumstances/with certain patients.
5. Explain what DIVA means in the veterinary vaccine world and advantages of using DIVA vaccines.
6. Explain the various factors that can be reasons a vaccine fails to protect.
7. Describe how you would investigate a vaccine failure, include what you would evaluate and give possible explanations for failure
8. Describe the mechanistic basis and expected timing for adverse vaccine reactions
9. Based on the Moore studies, explain what factors are associated with increased adverse vaccine events in dogs.
10. Describe the complexities associated with determining the duration of immunity for a vaccine and describe how it is determined in human medicine.
11. List factors that impact duration of immunity in an individual animal.
12. List and explain the mechanisms of maternal antibody interference with vaccination
13. List several factors that influence the response to vaccination in the presence of maternal antibody
14. Draw and label a graph that explains the reason for using a series of vaccinations in puppies and kittens
15. List several factors that can optimize vaccine efficacy and duration of immunity and minimize adverse reactions
16. Explain how an animal may have immunity but antibody to the agent is not detectable.
17. Describe the adaptive immune system protection of mucosal surfaces.
18. Describe how the immunity induced by an intranasal vaccine may differ from the immunity induced by a killed vaccine.

19. Describe how the immunity induced by an MLV oral vaccine may differ from the immunity induced by a killed vaccine.
20. Describe when and how a killed vaccine can stimulate lactogenic (IgA in milk) immunity to porcine epidemic diarrhea virus in a sow.
21. When given basic facts about a vaccine, use your knowledge of immunology to predict the type of immunity the vaccine would induce.
22. Describe the challenges of multifactorial diseases.
23. Illustrate and explain with a labeled drawing how it is often the additive effect of immunosuppressive factors that result in clinical disease and not one factor alone. Include at least two factors that decrease resistance to disease and one factor that will boost or increase resistance.

Principles of Veterinary Vaccinology Introduction

This set of lectures is designed to go along with the Principles of Veterinary Immunology online course. The target audience is veterinarians wanting information to help them make decisions regarding designing vaccination programs and to help understand why vaccines may sometimes fail to protect and may sometimes be associated with adverse events.

The course covers factors to consider when vaccinating animals because most often there is not one simple answer to questions about vaccinations. Veterinarians need to call on their knowledge and experience and weigh multiple factors related to a specific animal or herd, its history, and its environment when designing vaccination programs.

There is no such thing as a perfectly safe and perfectly effective vaccine; good vaccines are a balance of risks and benefits!

Risks of Vaccination

- Known vaccine-related side effects
  - Injection site-associated feline fibrosarcomas – a rare event; first identified in 1980s and originally was thought to be a result of vaccines injection but later determined that it could be any injection, not just vaccines. This began the discussion about the frequency of vaccination.
  - Hypersensitivities
    - Anaphylaxis
  - Nonspecific systemic side effects – common and transient, usually not serious
    - Fever, lethargy, loss of appetite a day or so after vaccination due to proinflammatory cytokine production occurs 12-28 hours after vaccination
  - Localized reactions at the injection site
- Alterations in immune homeostasis – do vaccines contribute to these situations?
  - Allergy in predisposed animals?
  - Autoimmune disease in predisposed animals?
  - Post-vaccinal polyneuropathy – Guillain-Barre syndrome in humans, coonhound paralysis in dogs

Always be aware of, and minimize potential risks, but, in general, the benefits of vaccinating with the core vaccines outweigh the risks

Benefits of Vaccination

- Vaccines are essential for:
  - Safe and efficient food production

- Control of emerging and exotic diseases of animals and people
- Control of zoonotic diseases, e.g. rabies
- Reduction of transmission of food borne disease, e.g. salmonellosis in poultry,
- Reduction of animal suffering
- Reduction of the need for antibiotics to treat animals
- Control of diseases of companion animals and horses

- Prevention of deadly diseases – e.g., core vaccines in companion animals prevent deadly viral diseases

Vaccination Principles Published by the AVMA Executive Board April 2001; revised April 2007)

- Introduction
  - "Selecting vaccine products and recommending vaccine programs are among the most complicated of medical decisions facing the veterinarian."
- Other highlights:
  - "Vaccine products vary in efficacy and safety and are not necessarily indicated for all patients."
  - "Vaccination protects a population of animals"… "Vaccination does not protect every individual patient even when they are properly vaccinated." (Herd immunity)
  - "Knowledge of immunology and vaccinology, including associated benefits and risks, and the pathobiology of infectious diseases, are necessary to implement an effective vaccination program."
- Conclusion
  - "Revaccination recommendations should be designed to maintain clinically relevant immunity while minimizing adverse event potential."

Basis for Protective Immunity

Introduction

- The pathogenesis and virulence factors of an organism are important factors for determining what type of immune response will provide the best protection to disease.
- Usually, the best immunity to a disease is recovery from disease. Vaccination tries to mimic immunity induced by the natural infection while sparing the animal the clinical disease and illness associated with natural infection.

Types of Immune Responses to a Pathogen Include:

- Humoral response:
  - Circulating antibody = IgM and IgG
  - Mucosal antibody response
    - IgA on the mucosal surface
    - IgE just under the mucosal surface located on mast cells
- Cell-mediated response:
  - Cytokine secretion - a complex mixture of various cytokines
    - Example - TH1 (CD4+) cell cytokines
      - Interferon gamma (IFNγ), tumor necrosis factor (TNF), interleukin 2 (IL2)
      - Enhance cell mediated immunity by activating macrophages, neutrophils, NK cells, and TC cells
  - Cytotoxic T cells (TC cells/CD8+)– recognize foreign antigen and MHCI and directly kill infected cells
  - Gamma delta (γδ) T cells – help protect mucosal epithelium, may act more quickly after initial exposure than CD4 and CD8 T cells

- Important antigens: Organisms have many antigens but only a few are important for inducing a protective immune response.
- When you know about the pathogenesis of the organism, you can make a good guess about what is needed for a protective immune response.

Examples of Pathogenic Mechanisms and Protective Defensive Mechanisms

Pathogenic Mechanisms	Defensive Mechanisms	Some examples
Adherence to mucosa	Mucosal antibody (IgA)	E. coli, enteric viruses
Helminthic parasites	T_H2, IgE	Roundworms, hookworms
Exotoxin/Endotoxin (LPS)	Neutralizing antibody	Tetanus toxin (exotoxin), Lipopolysaccharide (LPS) (endotoxin)
Viremia	Neutralizing antibody	West Nile virus
Septicemia	Opsonizing antibody - enhance phagocytosis	Extracellular bacteria: *Staphylococcus, Streptococcus*
Intracytoplasmic growth	Cytotoxic T cells	Intracellular bacteria and viruses
Rapid virus replication	Interferons – Type I and Type II	Viruses that spread more quickly than the immune response can produce antibodies , e.g. rhinoviruses
Intracellular growth/ growth in phagosome	T_H1 cytokines – e.g. IFNγ	Any virus that grows inside the cell, *Mycobacteria, Brucella*
Infect epithelial cells	γδ T cells - especially at mucosal surfaces	

Bacterial Antigens

Bacterial Antigens	Important Considerations in Vaccine Development
External • Pili • Flagella • Capsule	• Antibody important to block adherence • Antibody can opsonize for phagocytosis
Internal • Important antigens vs not important	• Antibody not protective (does not get inside of cells) • Cell-mediated immunity (CMI) may be important
Secreted • Exotoxins	• Need growth conditions that result in secretion of important factors • Neutralizing Ab is important
• Endotoxin - lipopolysaccharide (LPS) on gram negative bacteria	• Neutralizing antibody