SAND2012-8477P

Vaccine

EFFICACY AND USE

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Vaccine Efficacy

- **Antigen dose must be sufficient to induce an appropriate immune response**
- **Antigen presenting cells must be stimulated**
  - Critical for antigen processing
- **T & B cells have to be stimulated to generate memory cells**
- **T cells must be stimulated to initiate cell mediated response**
- **Helper and Effecter T cells must be generated to multiple epitopes**
- **Antigen has to persist in lymphoid tissue**
  - Duration of antibody generating cell stimulation
  - Duration of protection

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Ideal Vaccine

- **Highly antigenic**
- **Low side effects**
- **Lasting immunity**
- **In some cases, stimulation of the immune system can have negative side effects**
  - Modified live vaccines can revert to virulent strain or cause mild symptoms
  - Modified live vaccines can cause injection site reactions
  - Adjuvants for killed vaccines have caused severe local skin reactions (including induction of tumors in cats and dogs)

Live or Modified Live Vaccines

- **Very effective**
  - Most require only dose
    - **Not always the case**
  - Very good protection
    - **Rapid**
    - **Long lasting**
    - **Broad spectrum**
- **Requires less antigen**
  - Smaller volume
- **Few reactions**
- **Less expensive**
- **Stimulates Cellular Immunity**

Live or Modified Live Vaccines

- **Modified live vaccines can revert to the more virulent strain**
- **Side effects can include infection, death, abortion, and infertility**
- **Requires special handling and storage**
  - Heat sensitive
  - Easily inactivated
    - **Inflammation**
    - **Disinfectants**
    - **Contaminants**
- **Injection technique critical**
- **Booster vaccination recommended**
- **React to vaccine contaminant**

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Toxoids and Bacterins

- Are usually very safe
- Stable and convenient storage
- Require no mixing
- No risk of disease or infection
- Designed to stimulate antibodies against toxins and bacteria
- Unlikely to have contamination
- Requires boosters to sustain immunity
- Slower onset of immunity
- Can cause hypersensitivity
  - Injection site reaction
- Requires more volume

Adjuvants

- **Adjuvants maximize the effectiveness of vaccines**
  - Especially those that contain poorly antigenic killed organisms
- **Adjuvants can increase the sped or the magnitude of the bodies response to vaccines**
  - Less antigen is required to elicit the same response
- **Mechanism of action of adjuvants is poorly understood**
  - Reduce absorption to the vaccine to prolongs the immune stimulation
  - Directly stimulate the immune system
- **Five types of adjuvants exist**
  - Depot
  - Microbial
  - Immune stimulators
  - Delivery systems
  - Mixed

Adjuvants: Depot Adjuvants

- **Delay the elimination of antigen**
  - Once antigen is eliminated the immune system is turned off
  - Prolongation of antigen life can enhance the immune response
- **Aluminum salts when combined with antigen and injected form macrophage rich granulomas**
  - Antigen is slowly leaked into the body to provide prolonged stimulation
  - Antigens that exist for only a few days can remain active for a several weeks
  - Only influence the primary response
  - Do not stimulate cell mediated immunity
- **Freund's incomplete antigen**
  - Mixture of oil and water
    - **Stimulates local inflammation and the formation of a granuloma or abscess**
    - **Oil is irritating – irritation is not acceptable in modern vaccines**

Adjuvants: Immunostimulatory

- **Enhance immune response to vaccine by promoting the production of inflammatory cytokines**
- **The adjuvant looks like a pathogen associated microbial protein and therefore stimulates macrophages to produce cytokines**
  - Interleukin 1 and 12
  - Promote T helper cell activity
  - Enhanced T helper activity enhances antigen presentation and the subsequent response to antigen
- **Particulate matter from killed bacteria is also used**
  - Some can promote both antibody and cell mediated responses

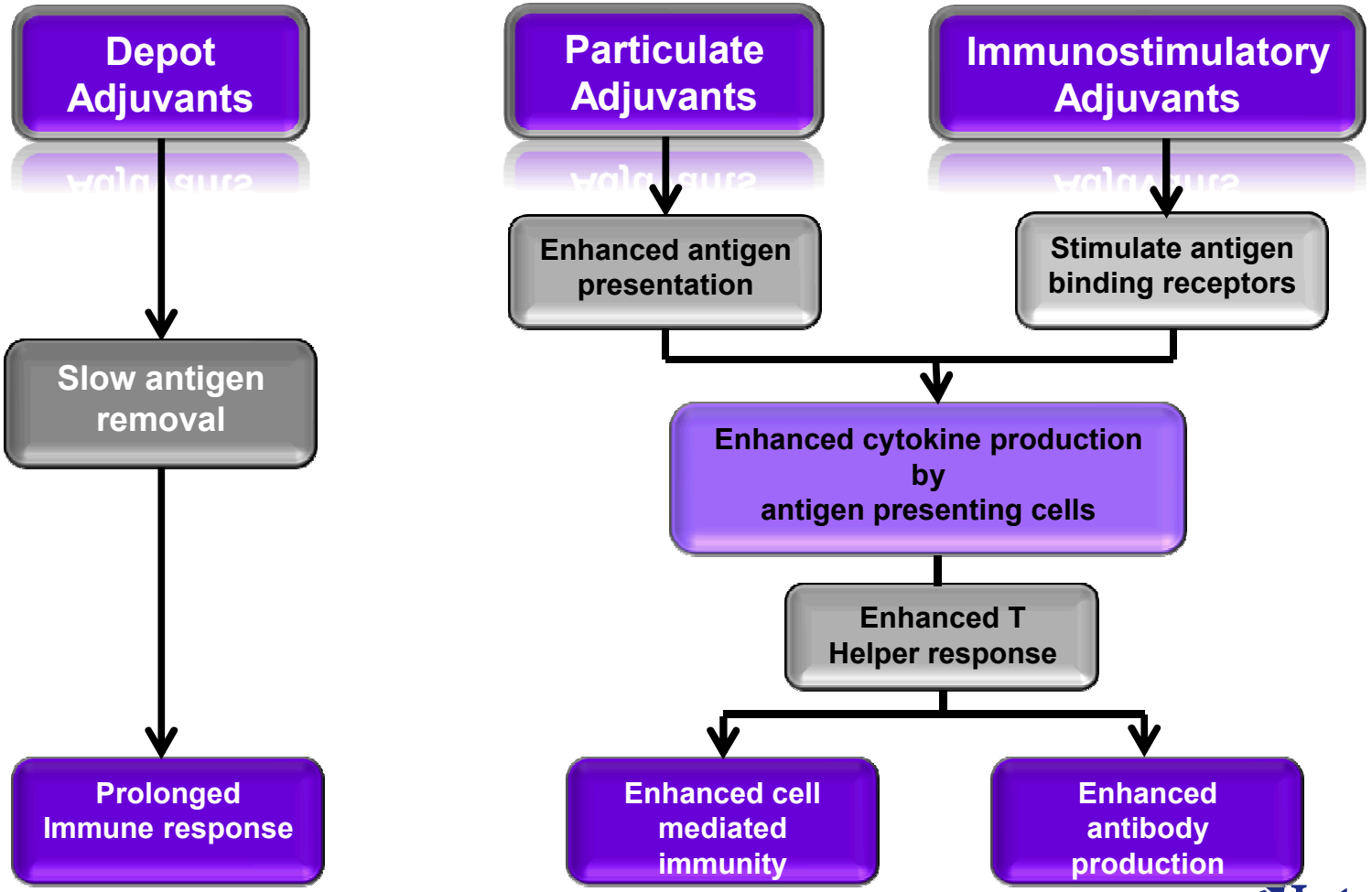
Adjuvants: Particulate

- **Particulate delivery systems can help immune system cells trap particles containing antigen more efficiently than if the antigen is alone**
- **These adjuvants are usually of similar size to bacteria and are easily phagocytized**
  - Liposomes are effectively trapped and easily processed
- **New technology that is not widely used**

Adjuvants: Combined

- **Very effective adjuvants can be constructed by combining a particulate adjuvant with a depot or immunostimulatory adjuvant**
- **Freund's Incomplete Adjuvant is a combination of oil and water with killed Mycobacterium tuberculosis**
  - Best when give subcutaneously or intradermally
  - Inhibits tolerance
  - Favors delayed response
  - Accelerates graft rejection
  - Promotes tumor resistance

Adjuvants: Review



Adjuvants

- **Depot effect to reduce absorption of killed vaccine and prolong duration of exposure**
- **Induce granuloma at vaccination site**
- **Effective with primary immune response but not secondary**
- **Aluminum salts**
  - Forms a macrophage-rich granuloma
  - Very stable vaccine, convenient handling for rural areas
- **Oil based adjuvants**
  - Sometimes include oil-in-water- Freund's incomplete
  - Oil has been predominant for FMD

Use of Vaccines

- **Vaccine administration should only be done after carefully assessing the risks and benefits of use**
- **Vaccines should be administered only in the dose and by the routes recommended by the manufacturer**
- **Vaccines should not be given more often than recommended by the manufacturer**
- **Vaccines may cause adverse reactions, so be prepared to address them should they arise**

Vaccine Handling

- **Minimize exposure to ultraviolet light**
- **Keep cool depending on formulation**
  - Some are more heat sensitive than others
- **Only pull out the amounted needed for a short amount of time**
- **Change needles frequently**
  - Prevents contamination and disease transmission
  - Replace dull or bent needles
    - **Reduces tissue damage and injection site reaction**
  - New needle for filling to prevent contamination of the vial
  - Use correct sized needles
- **Use clean syringes**
  - Disinfectant can inactivate modified live pathogen vaccines
- **Use according to label**

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Administration Techniques

- **Technique is important to ensure vaccine effectiveness**
- **Most vaccines are administered by injection**
  - All needles must be clean and sharp to reduce local inflammation and the risk of introducing infection
- **Vaccines are provided in a standard dose and this dose should always be administered independent of size**
  - The dose provided is the amount of antigen necessary to induce the cells of the immune response and initiate an immune response
  - Doses are not based on weight or size
    - **Very small animals may need a reduced dose to prevent adverse reactions**
- **Proper route of administration**
  - Intramuscular
  - Subcutaneous
  - Oral
  - Intranasal

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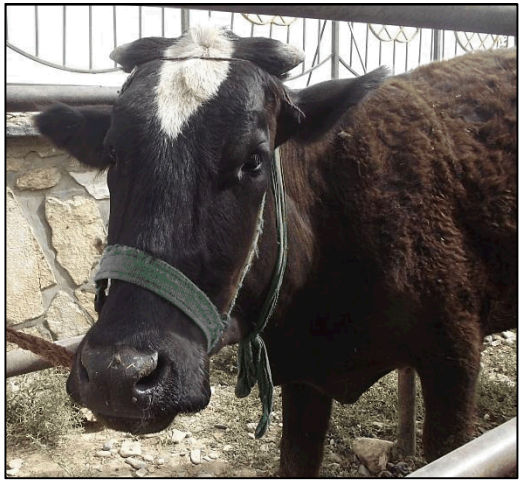
Administration Techniques

- **Most vaccines are given intramuscularly or subcutaneously**
- **In cattle and ruminants it is important to minimize injection site reactions in animals intended for consumption**
  - Ideally the front of the shoulder
- **In horses the front of the shoulder or hind limb muscles can be used**



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Vaccination Schedules

- **Schedules of specific vaccines may vary but certain scheduling principles are common to all methods of active immunization**
  - Initial series where protective immunity is initiated
  - Revaccination or booster shots at intervals

- **Initial series are given to young animals to induce immunity as soon as possible but also account for interfering maternal antibodies**
  - Passive immunity must be at a minimum
  - Difficult to predict, so a series is administered
  - Mostly in small animals

Vaccination Schedules: Revaccination

- **Revaccination (booster)**
  - Induction of memory, prolongation of response, and more robust antibody production
  - Maintain immunity over a period of time
- **Older vaccines may have required revaccination after six months**
- **More modern products may require yearly revaccination**
  - New rabies vaccines can be given every three years
  - Some vaccines provide life long immunity after initial series or dose but few reliable studies have been done to confirm
    - **Pestes des petits ruminants (PPR)**
    - **Rinderpest**
  - Annual revaccination is typically the rule for most animal vaccines

Vaccination Strategies

- **Vaccination alone may be infective to control a large outbreak of infection disease unless coupled with an effective strategy**
- **Success depends on:**
  - Selection of the right population to vaccinate
  - Determination of numbers to be vaccinated
    - **Proportion of animals vaccinated and vaccine efficacy**
    - **Neither will reach 100 percent**
- **Strategy depends on the rate the pathogen spreads**
- **Prophylactic administration can prevent large outbreaks by reducing the size of the susceptible population**
  - Identify high risk animals and populations

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Vaccination Strategies (continued)

- **Vaccination in the face of an outbreak is challenging**
  - Prophylaxis is preferable if feasible

- **Impossible to vaccinate the entire population**
  - Reactive vaccination strategies
    - **Ring vaccination**
      - Establish a barrier of protected animals
    - **Predictive vaccination**
      - Vaccinate the animals most likely to contribute to the spread of the disease
  - Try to shorten the duration of infection in a population

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Adverse Reactions

- **Residual virulence and toxicity**
  - Inadequate inactivation
  - Contamination with lipopolysaccharide
- **Allergic response**
- **Fever and generalized malaise**
- **Disease in immunodificient host**
- **Neurological complications**
- **Tumor growth in dogs and cats**
- **Harmful to fetus in pregnant animals**
- **Injection site reactions**
  - Can be severe

Vaccine Failures: Veterinary Professional

- **Use according to label to prevent veterinary professional vaccine failures**
  - Handle according to label
    - **Appropriate storage conditions**
    - **Mix suspension adequately**
  - Labeled dosage
    - **The dose provided is what is necessary to induce a protective immune response in a given population or species**
  - Expiration dates must be acknowledged
    - **Some vaccines are more sensitive than others**
  - Contaminated injection site
  - Failure to booster vulnerable populations
    - **Booster vaccines are important to ensure an adequate and long lasting response**

Vaccine Failures: Animal

- **Animal fails to respond - no vaccine is 100 percent efficacious**
- **Poor nutrition may result in a poor response to vaccine**
  - Animals need to be in good health to have an adequate response
- **Mineral, energy, and protein deficiencies reduce the effectiveness of vaccines**
- **Immunosuppression from disease, poor nutrition, poor housing conditions**
  - Incubating infection or diseased animals
  - Parasitized animals
  - Pregnant or lactating animals
  - Poor nutrition
- **Antibody interference**
  - Colostrum

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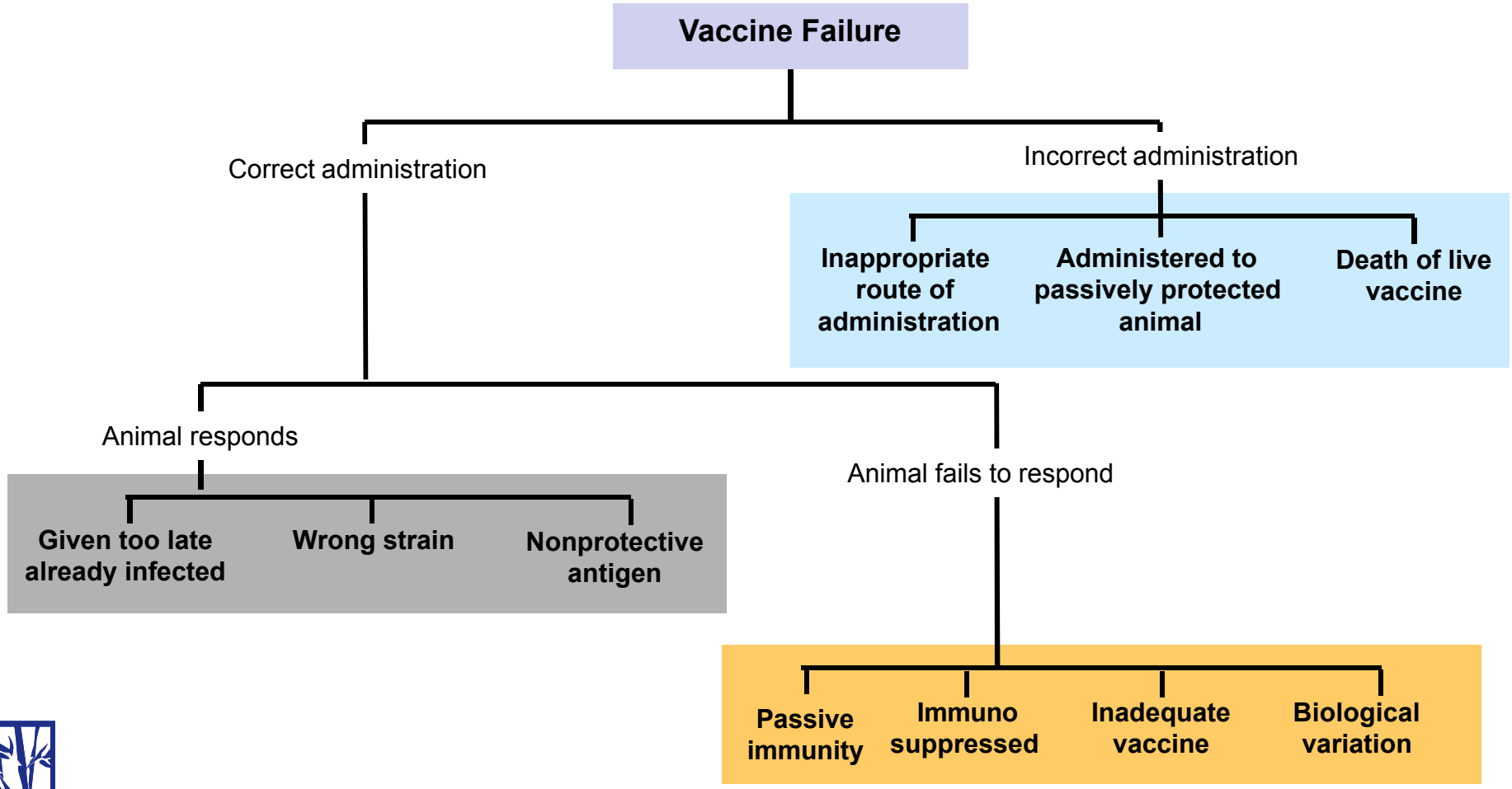
Vaccine Failure: Review



Group Activity: Part 1

- **Divide into 4 groups, designate a group leader, choose a vaccine**
- **You must address all of the below about your product**
  - Recommendations for use
    - **What strains?**
    - **What species?**
    - **What age?**
  - What type of vaccine – live, modified live, killed, subunit?
    - **What does that tell you about the immune response?**
  - What type of adjuvant is included?
  - What is the route of administration?
  - What is the dose to be administered?
  - What are the risks associated with use?
  - What are the risks to the administrator?
  - Are there different formulations?

Group Activity: Part 2

- **Stay in designated group**
- **Assume an outbreak has occurred in your district**
- **Develop a vaccination plan in response to the outbreak**
- **Consider**
  - Diagnostic testing practices?
  - Animal marking system?
  - What is the vaccine schedule for your population?
  - Strategy to employ for the outbreak?