Practical Disease Control in Dairy Herds

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Notes:

PowerPoint Slides on next page

Practical disease control in dairy herds- Making sure all three legs of the stool are standing

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Bovine Immunology Book

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https://bovineimmunity.hipra.com

2

Credits

- Slides
  - Kuby Immunology
  - Immunobiology, 8th edition
  - David Topham, University of Rochester
- Movies/Animations
  - Immunobiology, 8th edition

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Topics

- Overview-Disease Prevention
- What? Types of vaccines and pathogens/immunogens
- When? do we vaccinate- age and stressors
- How?- Route and Good Nutritional Plane

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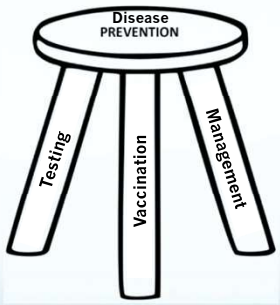
Disease Control Programs 3-Legged Stool



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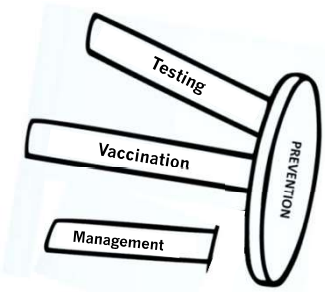
Disease Control Programs 3-Legged Stool



Must have all 3

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Homeostasis & the Immune System

- **Homeostasis** is the process by which a the animal maintains a stable, healthy internal environment.
- The **immune system** is part of the overall process of maintaining homeostasis.
- The immune system identifies and attacks harmful invasive biological entities called **pathogens**.

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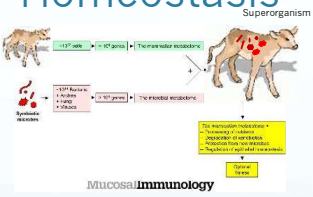
Homeostasis



Mucosal Immunology (2010) 3, 450-460

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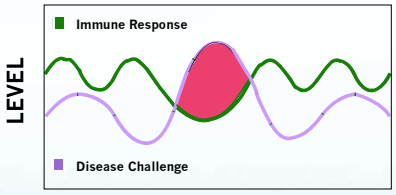
NOT ENOUGH OF A GOOD THING



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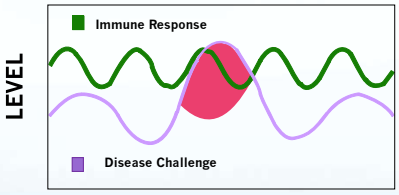
INFLAMMATION AND DISEASE- MAINTAIN HOMEOSTASIS-STEADY STATE



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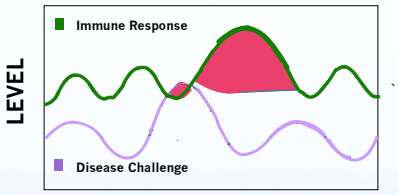
TOO MUCH OF A GOOD THING



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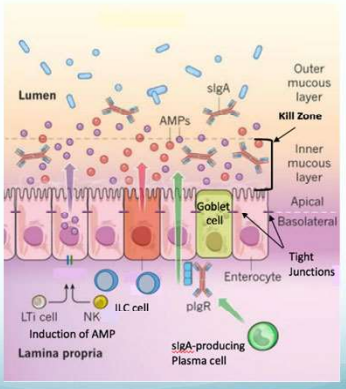
Epithelium and Kill Zone



Hydration- Key to Success

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Microbes and Regulating Body Systems

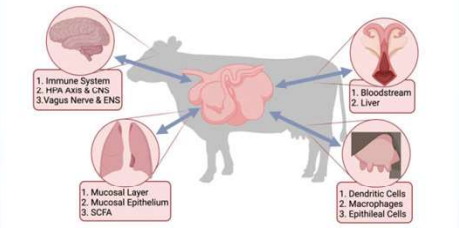

Figure 1. Proposed links between the gastrointestinal tract microbiota and different organ systems through the microbiome-gut-organ axes, including the microbiome-gut-brain axis (MGOA), the microbiome-gut-lung axis, the microbiome-gut-reproductive axis, and the microbiome-gut-mammary axis. Included are pathways, cells, and metabolites important for the bi-directional communication of the MGOA.

Clemmons, B.A., Voy, B.H., Myer, P.R., 2019. Altering the Gut Microbiome of Cattle: Considerations of Host-Microbiome Interactions for Persistent Microbiome Manipulation. Microbial Ecol 77, 523–536. https://doi.org/10.1007/s00248-018-1234-9

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Development of the Gut Microbiome

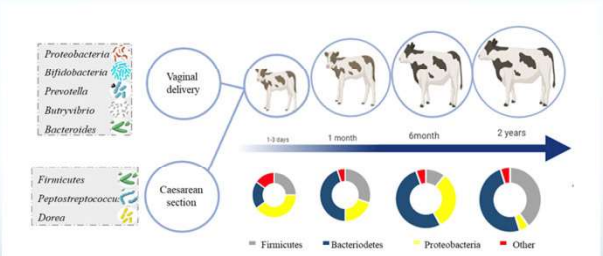

Figure 1. Dynamics of bacterial communities across different ages [24,32].

Khalil, A., Batool, A., Arif, S., 2022. Healthy Cattle Microbiome and Dysbiosis in Diseased Phenotypes. Ruminants 2, 134–156. https://doi.org/10.3390/ruminants2010009

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Microbiome- Different Organ Systems

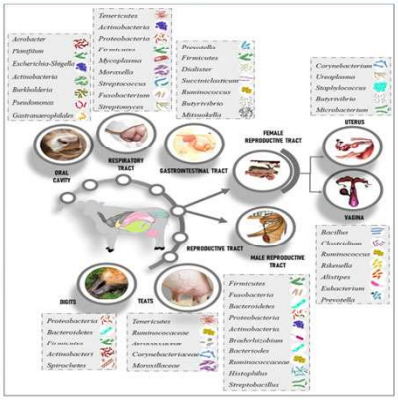

Figure 2. Variation in healthy cattle microbiome at different organs. Predominant bacteria in skin, reproductive organs, oral cavity, gastrointestinal tract, and respiratory tract are shown [10,13,35,40,51,55–57,60,62].

halil, A., Batool, A., Arif, S., 2022. Healthy attle Microbiome and Dysbiosis in Diseased henotypes. Ruminants 2, 134–156. https://doi.org/10.3390/ruminants2010009

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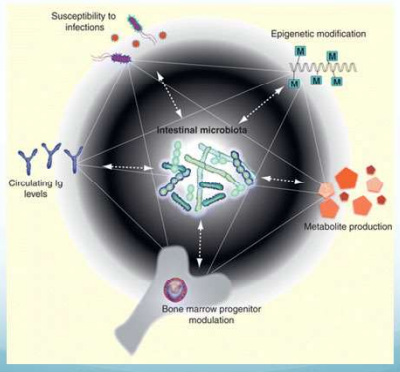
Microbiota and Immune Development

Global Effect of Microbiota



Reynolds, L. A., & Finlay, B. B. (2013).. *Expert Review of Clinical Immunology*, 9(11), 1019-1030.

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Take Aways

- Microbiome needs to be managed and not upset- diet, dehydration, intakes
- Pre- and Probiotics- where do they fit in?

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Take Home: A Healthy Gut is a Necessity- What About Probiotic and Prebiotics?

- Bacterial cultures, Yeast, cell wall products are good for gut health
- Problem: how do we measure it
- Do we need them all the time? No- times of stress

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Stress

- Stress is anything that reduces immune response capability
- Adaptation to intensive production is stressful
  - Anything that improves adaptation will reduce costs and improve production
- The reason that this condition is seen more in intensive operations rather than extensive

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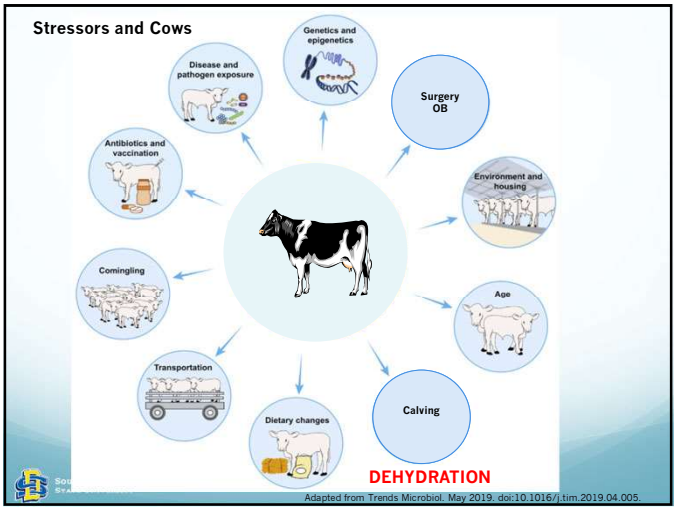

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Stress and Dysbiosis

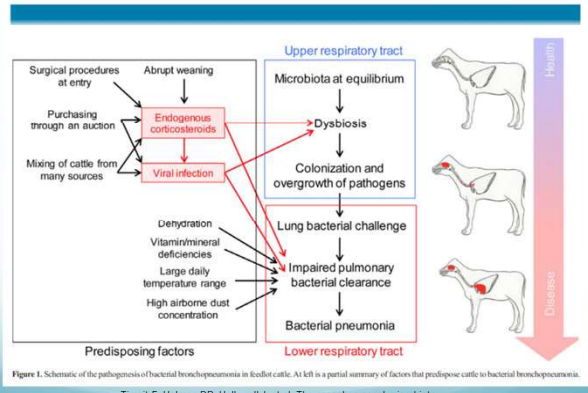

Figure 1. Schematic of the pathogenesis of bacterial bronchopneumonia in feedlot cattle. At left is a partial summary of factors that predispose cattle to bacterial bronchopneumonia.

Timsit E, Holman DB, Hallewell J, et al. The nasopharyngeal microbiota in feedlot cattle and its role in respiratory health. Animal Frontiers 2016;6:44–50.

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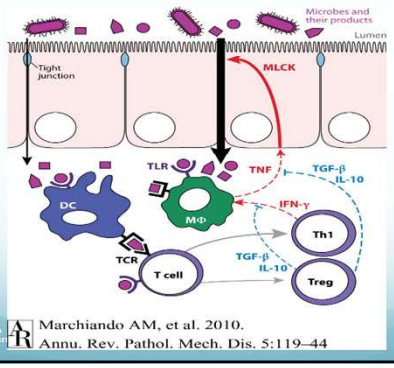
Inflammatory Response- Epithelial Cells



Marchiando AM, et al. 2010. Annu. Rev. Pathol. Mech. Dis. 5:119–44

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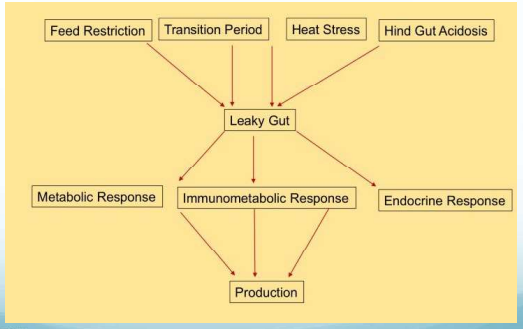
Leaky Gut

- Leaky gut explains the negative consequences of heat stress and off-feed events (all farm animals)



Baumgard L, International Symposium on Dairy Cattle Nutrition, Wageningen NL October 26, 2017

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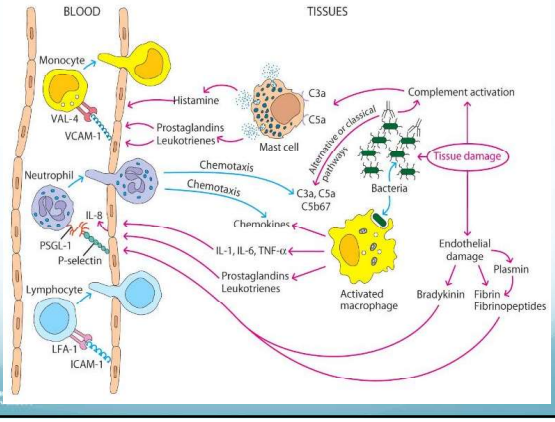
Inflammatory Response



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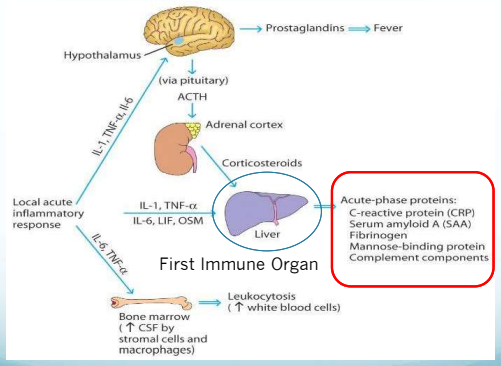
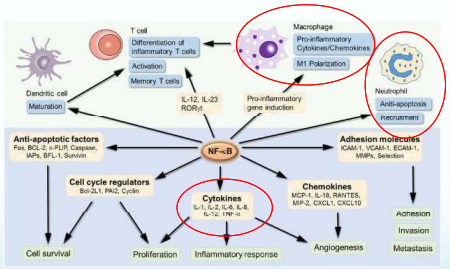
Inflammatory Response



Systemic response

Activation of NF-ΚB Pathway



Gut-Lung Inflammatory Axis

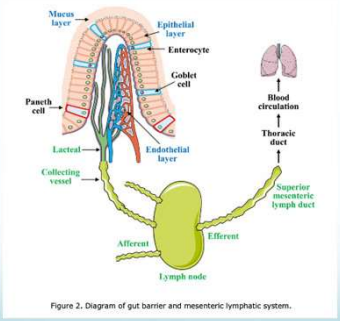


Figure 2. Diagram of gut barrier and mesenteric lymphatic system.

Ma, Y., Yang, X., Chatterjee, V., Wu, M., Yuan, S.Y., 2020. The Gut-Lung Axis in Systemic Inflammation: Role of Mesenteric Lymph as Conduit. Am J Resp Cell Mol. https://doi.org/10.1165/rcmb.2020-0196tr

Gut-Lung Inflammatory Axis

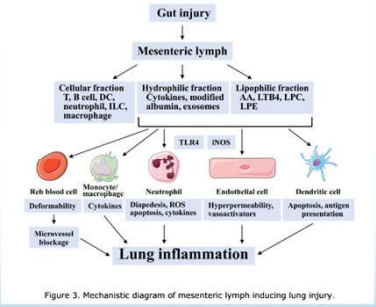


Figure 3. Mechanistic diagram of mesenteric lymph inducing lung injury.

Ma, Y., Yang, X., Chatterjee, V., Wu, M., Yuan, S.Y., 2020. The Gut-Lung Axis in Systemic Inflammation: Role of Mesenteric Lymph as Conduit. Am J Resp Cell Mol. https://doi.org/10.1165/rcmb.2020-0196tr

Inflammatory Cytokines

- Increase Sickness Behavior-listlessness
- Decrease feed intake- Inappetence-
- Increase body temperature sweats
- Decreased feed conversion
- Decrease gain
- Decrease milk production
- Increased Mastitis
- Increased Metritis
- Increased BRD

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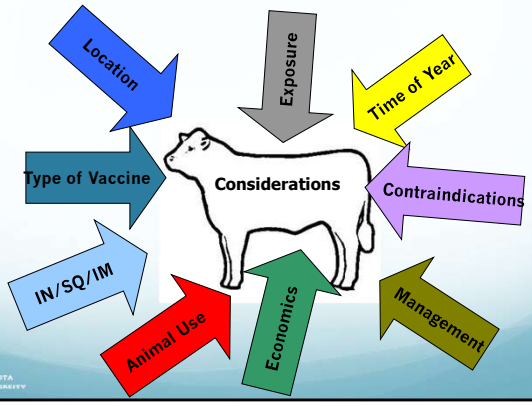
How do I Design a Vaccine Control Program?



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Goal of Vaccination is to Immunize
(Immunization versus Vaccination)

Vaccination: The act of administering a vaccine.

Immunization: An appropriate immune response following vaccine administration that provides protection from disease.

•There is a big difference between these two acts.
•Controlling environmental, pathogen and host factors will influence how many vaccinates truly become immunized.

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100% Guarantee- Biologically Impossible

- In most cases we hope that 70-80% respond and are protected
- In any herd, cattle or human, 100% of the vaccinates will not be protected
- With most viruses that is good enough.
- Herd Immunity

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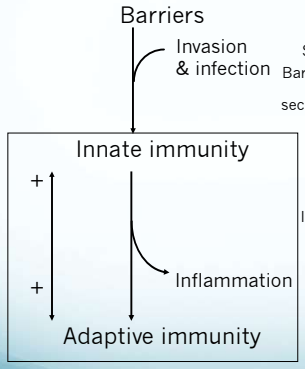
Immune Responses



•1st Line of Defense

•Barriers

Skin & Mucous membranes and secretions

Barrier, rapidly regenerating surfaces, peristaltic movement, lysozyme, sebaceous/mucous secretions, stomach acid, commensal organisms

2nd Line of Defense

Humoral and Cellular Components

Cellular, cytokine and protein defenses

Interferons, defensins, chemokines, cytokines (pro-inflammatory and T stimulatory), complement proteins, TLRs, phagocytosis, NK cells

3rd Line of Defense

Humoral and Cellular Components

Cellular and humoral defenses

Antibodies, cytokines, chemokines, T helper cells, cytotoxic T cells

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Herd Immunity

- How do you achieve Herd Immunity?
  - Vaccination
  - Exposure

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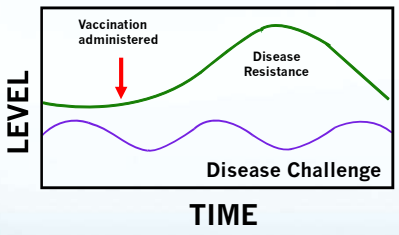
DISEASE AND RESISTANCE



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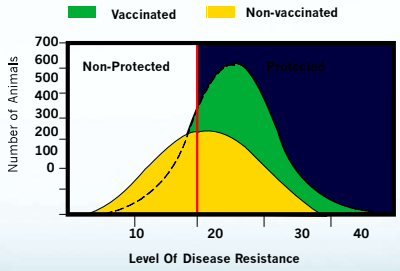
POPULATION DISTRIBUTION



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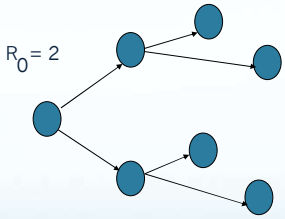
Basic reproduction number



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Herd Immunity Thresholds for Selected Bovine Vaccine-Preventable Diseases

Disease	R_0	Herd Immunity needed to prevent
BVDV PI	□	>95%
BRSV-naive	36.5*	>95%
BHV-1-naive	3.2##	75-86%
BVDV-Transient	0.25^-3.4**	70-80%
BRSV-endemic	1.14*	50-60%
BHV-1-latency	0.5^^	0%
COVID19	2-3	60-66%

*M.C.M. de Jong, W.H.M. Van der Poel, J.A. Kramps, A. Brand, J.T. Van Oirschot. 1996. Persistence and recurrent outbreaks of bovine respiratory syncytial virus on dairy farms, Am. J. Vet. Res. 57, 628-633.
#Bosch, J.C., Jong, M.C.M.D., Franken, P., Frankena, K., Hage, J.J., Kaashoek, M.J., Maris-Veldhuis, M.A., Noordhuizen, J.P.T.M., Poel, W.H.M.V. der, Verhoeff , J., Weerdmeester, K., Zimmer, G.M., Oirschot, J.T.V., 1998. An inactivated gE-negative marker vaccine and an experimental gD-subunit vaccine reduce the incidence of bovine herpesvirus 1 infections in the field. Vaccine 16, 265–271.
##Moerman, A., Straver, P.J., de Jong, M.C.M., Quak, J., Baanvinger, T., vanOirschot, J.T., 1993. A long-term epidemiologic study of bovine viral diarrhea infections in a large herd of dairy cattle. Veterinary Record 132, 622-626.
^^Sarrazin, S.,Dewulf, J., Mathijs, E., Laureyns, J., Mostin, L., Cay, A.B.,2014. Virulence comparison and quantification of horizontal bovine viral diarrhoea virus transmission following experimental infection in calves. The Veterinary Journal 202, 244-249.
□Brock, J., Lange, M., Guelberzu-Gonzalo, M., Meunier, N., Vaz, A.M., Tratalos, J.A., Dittrich, P., Gunn, M., More, S.J., Graham, D., Thulke, H.-H., 2020. Epidemiology of age-dependent prevalence of Bovine Herpes Virus Type 1 (BoHV-1) in dairy herds with and without vaccination. Vet Res 51, 124

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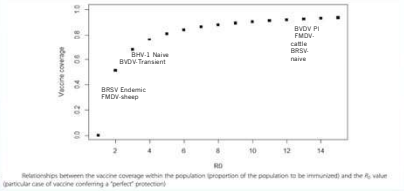
R_0- and Vaccination



Relationships between the vaccine coverage within the population (proportion of the population to be immunized) and the R_0 value (particular case of vaccine conferring a "perfect" protection)

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What?

Types of vaccines and pathogens/immunogens

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Types of Vaccines

- ✓ Killed or inactivated
- ✓ Modified-live or attenuated

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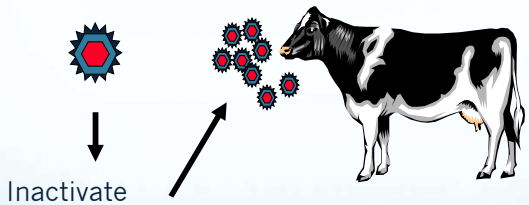
INACTIVATED (KILLED) VACCINES



Inactivate
- physical treatment
- chemical treatment

Fixed Antigenic Mass

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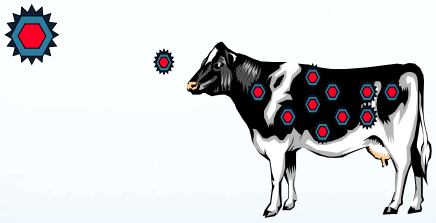
MODIFIED-LIVE VACCINES



Virus must multiply to generate antigenic mass

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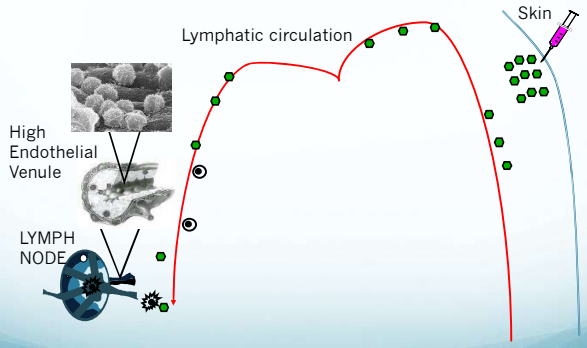
Vaccine Response in the Naïve Animal



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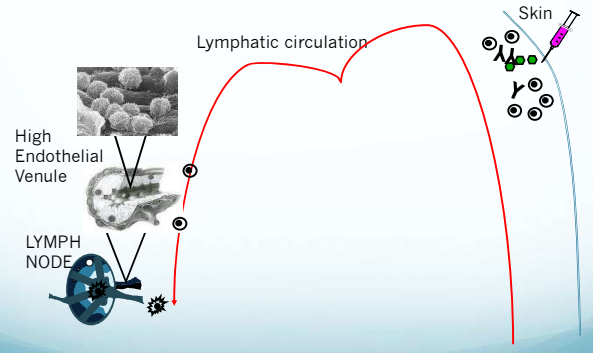
Vaccine Response in the Well-Protected Animal



Active Immune Interference- Never goes Away-Immune system doesn't know difference between vaccine and field virus

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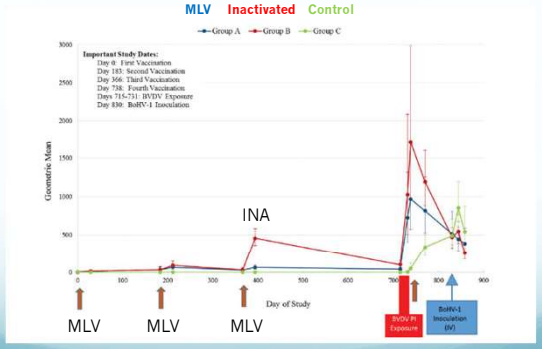
BVDV 1 Titers



Walz PH, Givens MD, Rodning SP, Riddell KP, Brodersen BW, Scruggs D, et al. Evaluation of reproductive protection against bovine viral diarrhea virus and bovine herpesvirus-1 afforded by annual revaccination with modified-live viral or combination modified-live/killed viral vaccines after primary vaccination with modified-live viral vaccine. Vaccine 2017;35:1046-54. https://doi.org/10.1016/j.vaccine.2017.01.006.

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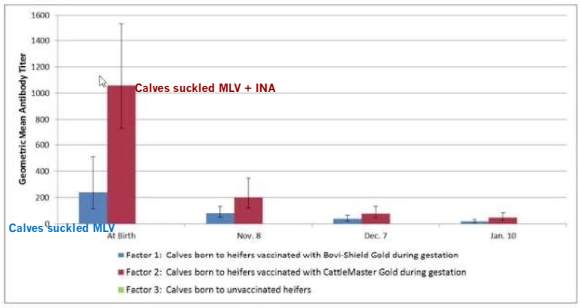
Transfer of Immunity to Calves



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What to Vaccinate with?

- In general, viral vaccine responses are better
- Many bacteria are endemic (*Histophilus somni, Mannheimia. hemolytica, Pasteurella. multicida, Moraxella spp., Mycoplasma bovis, Salmonella typhimurium, Clostridium perfringens)*

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What About Bacterins in Cattle?

- Site specific- Only if you have problem- many of these management related (nutrition, sanitation, environment)- efficacy is variable
- Clostridials
- Respiratory Pathogens
- Leptospira
- Salmonella
- Mastitis Vaccines

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What About Bacterins in Cattle?- Endotoxin Stacking

- Endotoxin Stacking and Vaccines (ranked most reactive to least reactive)
  - E.coli Mastitis vaccines
  - Pinkeye (Moraxella bovis)- Whole cell LOS very reactive
  - Histophilus somnus Whole cell LOS very reactive
  - Salmonella-Whole cell LPS
  - Scour vaccines E.coli-Whole cell LPS
  - Mannheimia hemolytica- Whole cell LPS
  - Pasteurella multicida
- Subunit vaccines- no issues, leukotoxin, fimbriae, OMP
- Leptospira DOES NOT contribute to ENDOTOXIN STACKING- leptospiral LPS does not have potent endotoxigenic properties
- If need to use more than one- administer on other side of the neck

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When?

Do we vaccinate- age and stressors

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What is your recommended viral vaccine protocol from birth to mature heifer?

- 1-3 days old: Intranasal vaccine with IBR-BRSV
- 8-12 weeks old: Intranasal vaccine with BRSV or MLV IBR-BVD-PI3-BRSV Heifers-LEPTO 5
- 4-5 months old: MLV IBR-BVD-PI3-BRSV-Heifers-LEPTO 5
- 7-9 months old: MLV IBR-BVD-PI3-BRSV-Heifers-LEPTO 5, must be 60 days prior to first breeding

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How?

Route, Booster Timing, and Good Nutritional Plane

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Intranasal vs Parenteral

- In face of maternal immunity- adjuvanted parenteral
- Mucosal immunity- Adjuvanted IgA
- Colostral Antibody- It Is not IgA- It's IgG-that comes from the serum- parenteral vaccines
- Reproductive viral vaccines- parenteral- prevent IBR and BVDV viremia

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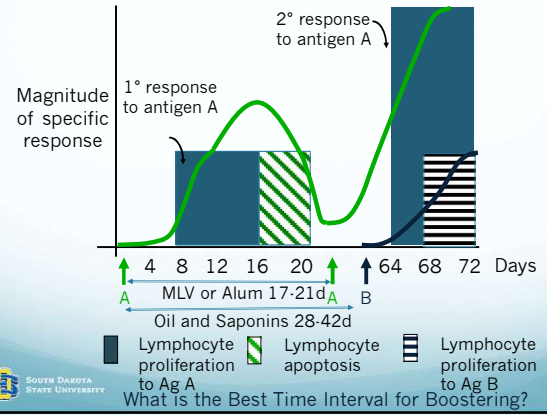
Timing and the Adaptive Immune Response- Anamnestic Response



What is the Best Time Interval for Boostering?

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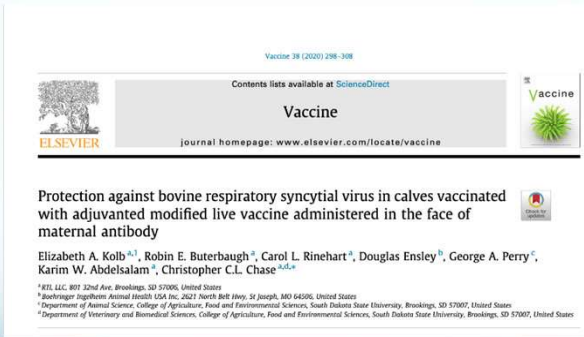
Vaccine 38 (2020) 298–308

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Protection against bovine respiratory syncytial virus in calves vaccinated with adjuvanted modified live vaccine administered in the face of maternal antibody

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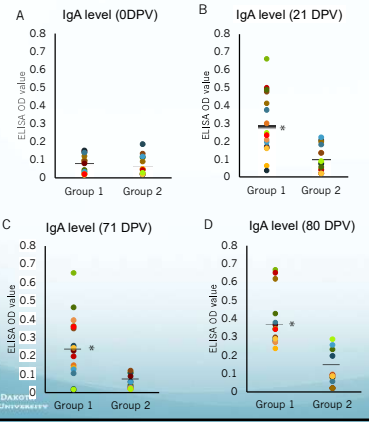
Nasal BRSV IgA



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Summary

- Parenteral- challenge 72 days after vaccination
- Rapid virus clearance
- Good memory from parenteral vaccine
- Less lung lesions
- Role for secretory IgG respiratory and reproductive disease

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Immunity and Energy

- Immune system doesn't get a free ride- energy consumer
- Multiple demands on energy for the postpartum cow

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Diet and Immune Response

Order of importance of nutrients to immune system

- Energy
- Protein
- vitamin A, D
- vitamin E
- Copper, Zinc, Selenium
- IRON

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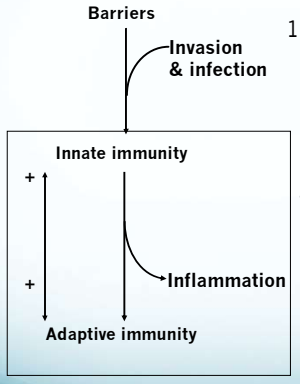
Immune responses



1st Line of Defense

Dehydration

2nd Line of Defense

Cellular and humoral defenses

interferon, cytokines (pro-inflammatory and T stimulatory), complement proteins, phagocytosis, NK cells

Dehydration

3rd Line of Defense

Cellular and humoral defenses

Antibodies, cytokines, T helper cells, cytotoxic T cells

From David J. Topham, Introduction to Viral Immunology:Part

Dehydration

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Points to Ponder in Developing Vaccination Schedules

- Vaccinate with What?
  - What are the disease problems on the farm or ranch?
- How Soon?
  - Immune Maturity
  - Route- IN vs Parenteral
- How Often?
  - Maternal Interference
  - Active Interference
- What type of vaccine?
  - MLV vs Inactivated
  - IN vs Parenteral

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Observations

- In general we vaccinate cows and calves too much and too soon
- On primary vaccination-if we vaccinate and we see nothing, nothing happened
- Interval for boosting needs to be 21 days or longer- length depends on vaccine

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Laws of Immunological Common Sense for Cows

- Vaccination of dams 4-6 weeks prior to calving improves colostral antibodies
- Vaccination of pregnant cows- two targets- calf and cow
- Vaccination of post-calving cow- wait at least 3-4 weeks after calving

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Take Aways

- Avoid turning on pro-inflammatory response at times of stress
  - Vaccination
  - Parturition
  - Weaning
  - Surgery
- Animals properly hydrated
- Can we modulate pro-inflammatory responses?
  - Using NSAIDS-Timing- Need to give before inflammation-
  - Need modulate initial pro-inflammatory response

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Harvey Dunn (1884-1952) Prairie is My Garden, South Dakota Art Museum

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