Calf Immunity: Expectations and Reality

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What We Know For Sure About Calf Immunity, and What We Wish We Knew More About

OR

What Might Work, and What Probably Won’t Work, When It Comes to Vaccinating Calves
Immune Development: Prenatal Calf

• Immune system begins developing before calf is born
  – Thymus (T cell development) evident at 40 days gestation
  – Response to some viruses possible at 70 days gestation
  – By third trimester, can respond to many different infections
    • At birth, see serum antibody titers elevated before colostrum intake

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• Few days before and after birth, immune responses of calf are suppressed
  – Maternal and fetal steroid production
    • Necessary to initiate calf birth BUT
    • Immunosuppressive
Immune Development, 
Neonatal Calf

• At birth, calf has no antibody in blood stream
  – Unless infected before birth

• Other issues
  – Serum antimicrobial proteins (complement) lower than adults
  – Immune cell functions slower and lower than adults

  – Become like adults by 5 – 8 months

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Immune Development, Neonatal Calf

• Immune response of neonatal calf is functional, but naïve and immature

• Colostrum is a solution to this problem
Calf Immunity:
Passive Antibody Transfer

• Adequate passive antibody transfer is arguably the most important factor influencing preweaning calf immunity
• Adequate colostrum intake is CRITICAL to calf health

• Calves without colostrum are
  – more likely to develop disease
  – more likely to die
  – more likely to fail to reach their potential for growth and production
Percent of dairy heifers with failure of passive transfer

<table>
<thead>
<tr>
<th>IgG Level (mg/mL)</th>
<th>Passive Transfer Status</th>
<th>Percent Calves</th>
<th>Standard Error</th>
</tr>
</thead>
<tbody>
<tr>
<td>More than 20.0</td>
<td>Excellent</td>
<td>52.4</td>
<td>(2.4)</td>
</tr>
<tr>
<td>15.0 to 20.0</td>
<td>Excellent</td>
<td>14.3</td>
<td>(1.2)</td>
</tr>
<tr>
<td>10.0 to 14.9</td>
<td>Adequate</td>
<td>14.1</td>
<td>(1.4)</td>
</tr>
<tr>
<td>6.2 to 9.9</td>
<td>Failure</td>
<td>8.0</td>
<td>(0.9)</td>
</tr>
<tr>
<td>Less than 6.2</td>
<td>Failure</td>
<td>11.2</td>
<td>(1.2)</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>100.0</td>
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</tbody>
</table>

19%

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• Before anything else, excellent passive transfer is required to establish the basis for strong calf immunity
How does nutrition impact immunity?
Nutrition and immunity

• Well known that nutrient deficiency impairs immunity
  – Protein and energy
  – Fat soluble vitamins
    • Vitamin A, D, E
  – Minerals
    • Copper, selenium, zinc, chromium

• Correct deficiency: improve immune response
• Supplement in excess: not always helpful
Nutrition and Calf Immunity

• Newborn Holsteins fed 50% of maintenance energy and protein
  – Decreased lymphocyte response to stimulation
  – Decreased ability to produce antibody following vaccination
• Correction of deficit: responses returned to normal

Griebel et al, 1987
Nutrition and Calf Immunity

- Effects of increased protein and energy
  - Calves fed 30% CP, 20% fat at 2.5% BW (DM basis)
  - Controls: fed 20% CP, 20% fat at 1.4% BW (DM basis)

- Interferon gamma and nitric oxide production by blood lymphocytes measured in both groups

  Nonnecke et al 2003, Foote et al 2005
Figure 6. In vitro effects of the plane of nutrition mitogen-induced interferon gamma (IFN-γ) synthesis by peripheral blood mononuclear cells (PBMC) from milk replacer-fed calves. Mean (± SEM) responses of PBMC from control (○) and high plane of nutrition calves (●) to pokeweed mitogen (a) and concanavalin A (b) are shown. Asterisk indicates control and treatment means differed (P < 0.05) on that specific day. Corresponding responses of adults (mean ± SEM, n = 6) PBMC are shown in the lower right hand corner of each panel.

Figure 7. In vitro effects of the plane of nutrition mitogen-induced nitrite produced by peripheral blood mononuclear cells (PBMC) from milk replacer-fed calves. Nitrite is the stable product of the oxidation of nitric oxide, and the amount of nitrite present in culture supernatants is indicative of the amount of nitric oxide produced by the PBMC. Mean (± SEM) responses of PBMC from control (-○-) and high plane of nutrition calves (●) to pokeweed mitogen (a) and concanavalin A (b) are shown. Asterisk indicates control and treatment means differed (P < 0.05) on that specific day. Corresponding responses of adults (mean ± SEM, n = 6) PBMC are shown in the lower right hand corner of each panel.
• Significance of these findings?
  – Both interferon gamma and nitric oxide are important for effective immunity
  – Both can be harmful in excess

• Not clear if calves fed more had immune advantage or disadvantage
  – More research needed to evaluate effect on disease
• Nutrition and immunity, summary:
  – Severe or chronic deficiencies impact immunity
    • Defects can be reversed if deficiency corrected early
  – Short term or moderate deficiencies may not impact immunity
  – High protein/energy diet does not clearly improve immune response
  – Need more research re impact on disease

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• Nutrition and immunity, questions
  – If calves are fed for biologically normal growth, will they automatically be prepared to optimally resist disease?
  – Could feeding more of any nutrient be *bad* for immune function or disease resistance?
    • High energy diets and respiratory disease: feedlot cattle

  – What (if any) *in vitro* measures of immunity best predict resistance to disease?

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Can supplements improve immunity and resistance to disease?

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Study #1

- Effect of fish oil supplementation of milk replacer (MR) on immune function
  - 51 Jersey bull calves
  - Fed 23% CP, 18% fat MR with 2% extra fat as either
    - 3:1 corn:canola oil
    - Half corn: canola oil, half fish oil
    - Fish oil only
  - 150 mg vitamin E added
- Calves fed to gain 200, 400, then 600 g/d in weeks 1-2, 3-4, and 5-6

Ballou and DePeters JDS 91:3488, 2008
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Fish oil supplementation of milk replacer and white blood cell function

Control:  Blend:  Fish oil:  

Ballou and DePeters, 2008

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Effect of fish oil supplementation on response to vaccination (d.0) and booster (d. 14)

Control: ○
Blend: △
Fish oil: □

Serum
1:50
Serum
1:200

Ballou and DePeters, 2008
• No effect of fish oil supplementation on growth or occurrence of diarrhea or respiratory disease
Study #2

- Effect of yeast culture on calf health and immunity
  - 512 Holstein calves divided into 2 groups
    - 2% yeast culture (*Saccharomyces cerevisiae*) in grain
    - No yeast culture
  - Grain fed free choice through d. 70
  - Pasteurized milk fed through d. 60

Magalhães et al, JDS 91:1497, 2008
• Trend toward increased bacterial phagocytosis and killing by WBC of calves fed yeast culture

• No effect on antibody production to vaccination
From Magãlhaes et al, 2008

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• Calves fed yeast culture had
  – significantly fewer days of diarrhea
  – Significantly fewer days of treatment for any disease

• Did NOT have significantly different rate of respiratory disease
• Feeding yeast culture in starter had significant effect on health outcomes

• Not much effect on immune functions measured in the study

• Perhaps other immune functions not measured were more important?
• **Summary, feed additives and health and immunity:**

  – Feed additives sometimes improve immune function, but not always correlated with obvious health improvements

  – Sometimes improve health without improving measured immune functions

  – Best studies look at both immunity and health

  – Ask to see results to support any claims
Supplements, immunity, and disease—questions:

– Is there a feed additive that consistently improves disease resistance in preweaned calves?
  • Does the benefit of this additive outweigh the cost?

– What (if any) laboratory test of immunity best predicts important disease resistance?
  • Would this vary for different feed additives?
What about vaccination?

(With thanks to Valley Vet)
Why We Vaccinate Cattle

![Graph showing antibody levels and vaccination](image)

**FIGURE 14-5** The relative amounts of each immunoglobulin class produced during the primary and secondary immune responses. Note that IgM predominates in a primary immune response, whereas IgG predominates in a later response.

From Tizard, 2009
Vaccination and Maternal Antibody

• Vaccination in the face of maternal antibody (IFOMA) traditionally considered ineffective
Vaccination without maternal antibody

Antibody titer vs. Time

Primary response

Anamnestic (memory) response

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Antibody titer

Time

Vaccination with maternal antibody

No response

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Vaccination and Maternal Antibody

- Failure of calf’s antibody concentration to increase was considered to indicate failure of response to vaccination

- Maternal antibody thought to “bind up” vaccine and prevent immune response
Calf vaccination IFOMA

• Several studies indicate calves CAN respond to vaccination IFOMA
Vaccination IFOMA can prime for memory response when maternal antibodies are gone
Antibody titer

Time

Vaccination IFOMA can prolong antibody titers
Vaccination IFOMA can induce T cell responses even when antibodies don’t increase.
Vaccination IFOMA can decrease disease when calves are later exposed to infection.

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Preweaning calf vaccination, challenges and questions

• Vaccinating to control respiratory disease
  – Disease sometimes starts early
  – Immature immune system
  – Impact of maternal antibody
    • Multiple doses likely needed
    • How much is too much?

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Intranasal vaccination

• *May* be superior to injectable for calves with maternal antibody

• Need research!
  – Duration of immunity may be issue (for BRSV, at least)
Figure 1—Experiment 1, median rectal temperatures before and after BRSV challenge in approximately 4.5-month-old calves that had been previously vaccinated IN at 3 to 8 days of age with a combination vaccine containing modified-live BRSV (group A, 10 BRSV-seropositive calves; group B, 8 BRSV-seronegative calves) or with vaccine diluent (group C, 10 BRSV-seropositive calves). Error bars represent minimum and maximum rectal temperatures recorded for each day.
Vaccination IFOMA, field trials

• Most relevant measure of vaccine efficacy

• Expensive and logistically challenging to conduct
Field Trial Example #1

• 2882 dairy calves at 19 dairies in Minnesota and Ontario

• Calves vaccinated with MLV 5-way IM (Bovishield)
  – 2 weeks of age
  – 5 weeks of age
  – 2 and 5 weeks of age
  – Not vaccinated (control group)

• Producers recorded whether calves developed respiratory disease  
  
  Windeyer et al., 2010
• Overall, 19% of calves treated for BRD
  – Range of calves treated by herd: 0% - 37%
• BRD first seen
  – In 6% of calves < 2 weeks old
  – In 7% of calves between 2-5 weeks old
  – In 7% between 5 weeks and 4 months of age

• Rate of failure of passive transfer was low

• No difference in rate of treatment for BRD for any of the vaccine groups

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Field Trial #1, Key Points

• Important amount of disease already occurring before vaccines had time to take effect
  – But would have been hard to vaccinated calves much earlier!
• Low rate of FPT: maternal antibodies may have interfered with vaccine
  – Perhaps intranasal vaccine would have been more effective?
• Vaccinating part of calves in each herd decreased chance of seeing effect of vaccine (herd immunity)
Field Trial Example #2

• 27 dairy herds with calf respiratory disease in previous year
  – Evidence of BRSV infection in previous year in 20
• 9 herds: calves vaccinated with MLV BRSV twice at 4 to 5 week interval
• 8 herds: calves not vaccinated
• 10 herds: half calves vaccinated, half not
• Calves 2-10 months of age at vaccination
• Vaccinated in August

Verhoeoff et al., 1984
• Calves had low serum titers to BRSV at vaccination (78% had no BRSV antibodies)
• Calves examined by vet weekly from October to January
• BRSV infection occurred in
  – 6 of 8 nonvaccinated herds
  – 2 of 9 completely vaccinated herds
  – 9 of 10 partly vaccinated herds
• Signs of respiratory disease seen in
  – 4 of 8 nonvaccinated herds
  – 1 of 9 completely vaccinated herds
  – 1 of 10 partly vaccinated herds

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Field Trial #2, Key Points

• MLV BRSV vaccination associated with decreased disease in vaccinated herds

• INFECTION with BRSV was decreased only when all calves were vaccinated
  – Vaccinating half of calves decreased disease but not infection

• Calves got 2 doses of vaccine
  – Can’t say if 1 dose would have same effect
• Vaccination for respiratory disease, questions:
  – When should calves be vaccinated?
  – What agents should be in the vaccine?
    • Coronavirus??
  – How often should calves be vaccinated?
  – By what route should vaccines be given?
  – Can you vaccinate calves too much?
  – Do the answers to these questions differ for calves in different housing situations?

• Large dairies and heifer rearing operations could help answer these questions with properly designed trials
• Answers probably influenced by
  – Interaction of age, maternal antibody concentration, and nutrition
  – Degree and nature of challenge
    • High vs low concentrations of infectious agents
    • Multi-agent vs single agent challenge
    • Virulence of agents
  – Superimposed effects of other stressors
    • Weaning
    • Castration and/or dehorning
    • Mixing of calves from different sources
    • Weather extremes

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• All of these factors must be taken into account when developing vaccination programs for calves

• We often have to make an educated guess when developing plans for calves dealing with a variety of these factors
Summary

• Vaccination IFOMA can sometimes prime calves for useful (protective) immune responses

• We need more information on factors that limit efficacy of vaccination IFOMA
  – Particularly in calves < 1 month old

• All vaccines are not the same
  – Ask to see data to support any claims
Vaccinating calves: points to remember

• Calves are more likely than adults to require booster vaccinations
  – Booster: 2 to 4 weeks after the initial vaccination
  – Later may be acceptable

• IN vaccines may be more effective than SC/IM in calves with high concentrations of maternal antibodies
  – Immunity from intranasal vaccines may not last more than weeks to few months

• Repeated doses of intranasal vaccines may not boost as effectively as repeated doses of injected vaccines

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Vaccinating calves: points to remember

• Calves with high concentrations of maternal antibody may not respond to vaccination as well as calves with moderate to low concentrations

• **When vaccinating calves, plan to boost once or twice before disease is expected to occur**

• Try to administer vaccines so the final boost is given one month before expected disease
Take home messages

• Preweaning calves can respond to immune stimulation
  – As early as 1 day of life
  – Reliability of response inversely correlated with age

• Adult immune responses present by 5 – 8 months

• Vaccinating late gestation cows might improve immunity
  – Really need more research
Take home messages

• Maternal antibody blocks response to vaccination sometimes but not always
  – Blocking is greatest in first month of life
  – Calves 2 – 3 months old: more reliable response
  – Really need more field trials to provide guidance
Take home messages

• When vaccinating calves under 6 months of age, try to give at least 2 doses one month apart
  – More than that might be counterproductive
  – Try to time second dose 1 month before disease is expected

• Consult with your veterinarian regarding vaccine choice and timing
Case for Discussion

• Dairy milking 1600 cows

• Pneumonia in calves after they leave hutches and go to group pens at 4 weeks of age
  – 50% of calves treated for pneumonia in past month
  – 5 calves have died of 200 at risk

• Calves are given intranasal IBR/PI3 vaccine at 2 days of age

• Given IM MLV 5-way vaccine immediately before being turned into group pens

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Issues to address

• Review management
  – Colostrum delivery adequate?
    • Colostral antibodies should help decrease respiratory disease in first 4-6 months
    • Check total proteins on week old calves
      – want > 5.4 in not < 80%
  – Care while in hutch
    • Adequate body condition?
Management, continued:

– Hutches spaced so no nose-to-nose contact?
– Adequate air flow between hutches?
– Adequate separation from older calves/cows

Post-hutch management

– Groups not too large
– Aim for not more than 8 weeks (less possibly better) age spread among calves
– No nose-to-nose contact with older calves, heifers, cows

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• Review use of vaccines
  – Intranasal IBR/PI3 at 1 day of age
    • *May* be helpful for short time
    • Not enough for all of calfhood
    • Probably not necessary if adequate passive transfer
    • Does not include BRSV and other agents likely to be a problem
      – *Mycoplasmas*, *Pasteurella multocida*
• IM 5-way at move to group pens
  – Contains IBR, PI3, BRSV, BVDV types 1 and 2
    • More broad—good, but...
  – Single dose right before turnout doesn’t give calves time to respond
  – Need to move back 2 weeks
  – Consider 2 doses 2 weeks apart with last dose 2 weeks before turnout
  – If passive transfer good, intranasal vaccine (e.g., Inforce 3) might be better than intramuscular

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