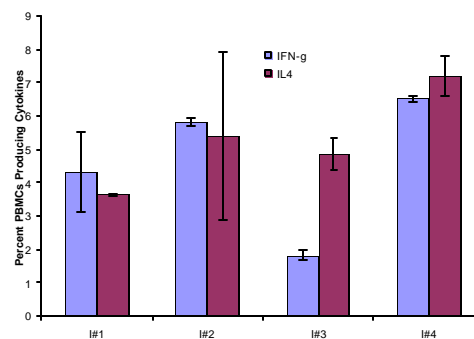


Vaccine-enhanced pathology in calves vaccinated with *Mycoplasma bovis* bacterins

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PBMCs from infected calves produced intracellular IL-4 and IFN- γ



Vanden Bush TJ, Rosenbusch RF: Characterization of the immune response to *Mycoplasma bovis* lung infection. Vet Immunol Immunopath 94: 23-33, 2003

New immune response paradigms

TH1 response to intracellular pathogen (inflammatory response) IFN- γ , IL-12, IgG₁

TH2 response to parasites (hypersensitivity response, smooth muscle contracting) IL-4, IL-10, IgG₂

TH17 response to extracellular pathogens (highly inflammatory response activates neutrophils, antimicrobial peptides) TGF- β , IL-17, IgA

Specific Treg cells modulate each response, stimulated by the same lymphokine that activated them

Vaccine effectiveness vs. transthoracic challenge-1

2 doses of oil-adjuvanted *M. bovis* bacterins confronted with heterologous challenge and necropsy at 8 dpi

Vaccine	Lung Score	Total score	Nr affected
A	9.7 \pm 2.7	10.7 \pm 3.2	4/5
B	11 \pm 3.5	12.2 \pm 3.6	4/5
C- placebo	3.2 \pm 1.5 *	4.6 \pm 1.6 *	1/5 *

An affected calf had total score > 7.5 (composite of clinical score + lung lesion score + lung burden)

Vaccine effectiveness vs transthoracic challenge-2

2 doses of aqueous-adjuvanted *M. bovis* bacterins confronted with heterologous challenge and necropsy at 9 dpi.

Vaccine	Lung Score	Total Score	Nr affected
I	10.4 ± 3.9	12 ± 3.8	3/5
II	11.9 ± 6.2	13.7 ± 2.9	4/5
Unvacc	9 ± 2.4	10.8 ± 2.6	4/5

Vaccine effectiveness vs 2X intranasal challenge-3

2 doses of aqueous-adjuvanted *M. bovis* bacterin confronted with heterologous challenge and necropsy at 11 dpi.

Vaccine	Lung score	Total score	Nr. affected
D	2.7 ± 0.2	10 ± 7.6	2/4
Control	3 ± 1	10.5 ± 8.7	1/4

Lung colonization was quantitated more precisely, lung lesions were less apparent in this trial.

Characterization of vaccine-enhanced pathology

Calves were vaccinated 3X with oil-adjuvanted bacterin or oil adjuvanted sham vaccine, then confronted with homologous challenge given intratracheal and necropsy was done at 4 and 11 dpi

Evaluation-

Gross Lung Lesions

Lung mycoplasma burden (pool of 15 lung sites)

Lung lymphocyte subset % (magnetic separation)

Specific lymphokine products from the subsets (Q-PCR)

6/5/09

Calves necropsied 4 days after challenge

- Sham vaccinated & challenged
 - Minimal lung lesions
 - Moderate lung burden
 - GD-WC1⁺ were predominant T cells
 - CD4 T cells committed to a TH17-like response
- Vaccinated & challenged
 - Heavy lung lesions
 - Heavy lung burden
 - CD4, CD8, GD-WC1⁺ were equally represented T cells
 - CD4 T cells committed to a TH1-like response

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Calves necropsied 11 days after challenge

- Sham vaccinated & challenged
 - Minimal lung lesion
 - Moderate lung burden
 - GD-WC1⁺ and CD8 were predominant T cells
 - CD4 T cells modulated down from a TH17-like response
- Vaccinated & challenged
 - Minimal lung lesions
 - Moderate lung burden
 - CD4, CD8, GD-WC1⁺ were equally represented T cells
 - CD4 T cells were anergic

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Conclusions

- Oil-adjuvanted bacterins cause vaccine-enhanced pathology after lower respiratory tract challenge
- VEP is associated with increased lung mycoplasma burden, early Th1 response, followed by anergy
- Enhanced lung lesions are seen early after challenge and then subside
- Neither oil-adjuvanted nor aqueous-adjuvanted bacterins induced protection against lower respiratory tract challenge

6/5/09