Infectious diseases of the newborn lamb

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Introduction

- Antibody response in the newborn
  - Epitheliochorial placentation
  - Lambs are agammaglobulinemic at birth
    - 0.3 mg Ig/mL vs 20 à 25 mg/mL in adults

- Importance of infectious diseases in lambs

~ 20 %

<table>
<thead>
<tr>
<th>% of total mortality</th>
<th></th>
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</thead>
<tbody>
<tr>
<td>Abortions</td>
<td>5.2</td>
</tr>
<tr>
<td>Dystocia</td>
<td>7.6</td>
</tr>
<tr>
<td>Lambing trauma</td>
<td>11.0</td>
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<tr>
<td>Mortinatality</td>
<td>18.2</td>
</tr>
<tr>
<td>Starvation hypothermia</td>
<td>34.1</td>
</tr>
<tr>
<td>Digestive infections</td>
<td>10.8</td>
</tr>
<tr>
<td>Respiratory infections</td>
<td>3.5</td>
</tr>
<tr>
<td>Other infections</td>
<td>5.2</td>
</tr>
<tr>
<td>Other non infectious</td>
<td>4.4</td>
</tr>
</tbody>
</table>

(From Johnston, 1980)
• Diversity of infectious diseases in lambs

- Birth
- 48h
- 7 days
- 21 days
- Weaning

- Infectious abortions
  - QFever, Chlam, Salmo, BD, toxo…

- Watery mouth disease, diarrhoea (E.Coli)
- Enterotoxemia (C. perfringens)
- Septicemic pasteurellosis (P. haemolytica)
- Cryptosporidiosis
- Enterotoxemia (C. perfringens)
- Arthritis
- Pasteurellosis (P. haemolytica)
- Pasteurellosis (P. haemolytica)
- Enterotoxemia (C. perfringens)
- Arthrites (E. rhusiopathia)
- Coccidiosis
Introduction

• How to control infectious diseases in lambs?

- Improve colostral (passive) immunity
- Improve innate / adaptative immunity
- Control environmental risk factors
Improve passive immunity

- Improve colostrum intake by lambs
  - Early drop off
    - of colostrum IgG1 concentration
  - of IgG1 absorption by epithelial cells
  - Lamb vigour
  - Ewes to lamb bonding
  - Genetic factors: FcRn....

- Improve colostrum quality and quantity
Variability of colostrum

- IgG1 colostrum concentration at lambing

![Graph showing IgG1 concentration distribution with peaks at 22.0%, 51.5%, and 26.5%]

- Effect of ewe age, litter size, udder health, nutrition...
  - Gilbert 1988, Mellor 1988, Snowder 1991...
Variability of colostrum

- IgG1 mass production over 12 hours in twins lambing ewes

- Colostrum and IgG1 quantity per lamb decrease as litter size increases
Improve colostrum quality and quantity

• Effect of nutrition
  – Energy and protein supply → BCS during gestation
  
  – Energy sources (Banchero 2004, 2009)
  
  – Effect of minerals and vitamins (selenium)
    • Supra-nutritional Se supply in late gestation in non deficient ewes
      – No effect or increase of colostrum yield (Swanson et al., 2008; Meyer et al., 2011)
      – No effect on IgG1 concentration (Swanson et al., 2008; Rock 2001)

  • Se adequate supply in deficient ewes in late gestation
    – Effect on IgG1 concentration: no effect (Corbière, 2013)
    – Effect on passive transfer of immunity: no effect (Corbière, 2013)
Improve colostrum quality and quantity

• Vaccination in late gestation
  – Specific protective Ab in colostrum
    • Higher plasma specific Ab concentration in newborn than in the dam
    • Not for all pathogens
      – +++ : E. coli (F5), Pestivirus, Rotavirus, E. rhusiopathiae, BTV8...
      – 0 to +++ : M. haemolytica, C. perfringens...
      – 0 : Parapoxvirus, Cryptosporidium...

  – Potential interferences between maternal Ab and active immunity in lambs
    • Well demonstrated
      – Clostridium perfringens ε toxin (de la Rosa, 1997)
      – BTV8 / inactivated vaccine (Oura, 2011, Leemans, 2013)
    • But poorly understood
      – Epitope masking, enhance clearance, cross linking with B cells, induction of Treg...
Improve colostrum quality and quantity

- **Genetic selection**
  - **Evidences**
    - Heritability of colostrum IgG1 mass produced: 0.45 (Hallyday 1978)
    - Heritability of colostrum IgG1 concentration: 0.19 (Gilbert, 1988)
  - **Implication of FcRn?** (Mayer, 2002; Lu, 2007)
    - FCGRT and β2M allele polymorphism in cows
      - increased default of TPI in their calves: (Laegreid, 2002) (Clawson 2004)
      - decreased colostrum IgG1 concentration: OR = 2.99 [1.31-6.83] (Zhang 2009) (Zhao, 2011)
  - **Impact on other production traits and immune responses?**
  - **Implication in sheep?**
    - On-going researches
Improve immunity in lambs

- **Immunity in newborn lambs**
  - Able to mount a cellular and humoral immune responses as early as at fetal stage, but of reduced strength
    - Low lymphocyte numbers
    - Low concentration of complement components (C3)
    - Low expression of CD86 and CD40 in Antigen presenting cells (APCs)
    - Reduced MHC II antigens presentation in APCs
    - Poor response to IFN-γ in Lymphocytes T
    - Poor response to LPS in macrophages and B cells...

- Immune response bias towards Th2
  - Reduced Th1 and Cytotoxic T lymphocytes responses
  - Progesterone and PGE2 effects in utero and around birth (IL-12 ➔ IL-10 ➔)
  - Cortisol effects at birth
    - Modification of cytokine production
    - Reduced MHC I antigen presentation in APCs
Immunity in newborn lambs

• The susceptibility window

- Depends on amount of colostral Ab
- Pathogen specific
Improve newborn immune response

• Vaccination in newborn should
  – overcome the materanl Ab obstacle
  – balance between Th1 Th2 responses
  – enhance mucosal immunity
    • Numerous licenced vaccines for poultry, horses, swine, dogs, cats, cattle
    • None in sheep

• Development of efficient adjuvants and Ag presenting strategies
  – Particle vectors
    • Nano-particles (Gamvrellis, 2013)
    • Immune Stimulating COMplexes (ISCOMs) (Morein, 2004)
    • CpG Oligodeoxynucléotide (CpG ODN)
    • ...
  – Live vectors
    • Virus, bacteria
  – Cytokines
    • IL-2, IFNg, IL-1, IRX-2, GM-CSF
Improve newborn immune response

- **Immunostimulation**
  - Poorly investigated in domestic animals
    - Poorly understood mechanisms
    - Conflicting results
  - Minerals, vitamins
  - Cytokines
    - Rb-IFNα1 and BHV-1/ *P. haemolytica* and *S. typhimurium* challenges in calves (Babiuk, 1987, Peel, 1990)
  - Probiotics
    - Yeast, viral or bacterial extracts (proteins, DNA...)
      - Eqstim®, Equimune® (Horse), Staphage®, Baypamum® (Dog)
Control environmental risk factors

• Environment of newborns (sheepfold or pastures)
  – Exposure to infectious pathogens
  – Influence host susceptibility to infectious diseases
    • Thermal stress
    • Social stress
    • Alimentary stress
    • ...

• Identification and control of risk factors
  – Improve sheepfold conception
  – Improve farmers’ practices
  – ..
Conclusion

• Considerable gaps in knowledge (particularly true in lamb)
  – Newborn immunity
  – Newborn vaccinology
  – Immune response stimulation

• Poor interest of pharmaceutical companies in research
  – Development of efficient lamb vaccines

• Back to basics
  – Colostrum production and intake
  – Control of infectious risk factors
Thank you for your attention