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Infectious diseases of the newborn lamb

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- **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

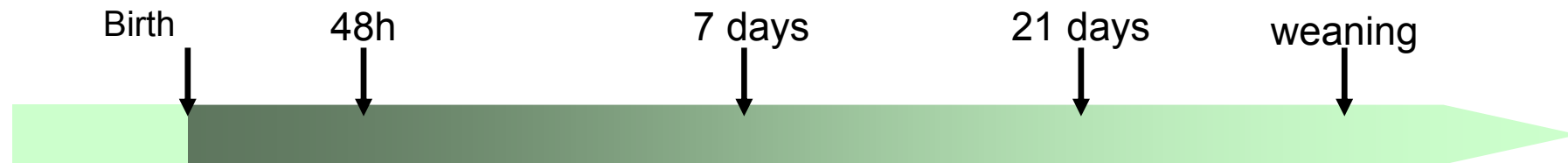
- **Importance of infectious diseases in lambs**

~ 20 % ←

% of total mortality	
Abortions	5.2
Dystocia	7.6
Lambing trauma	11.0
Mortinatalité	18.2
Starvation hypothermia	34.1
Digestive infections	10.8
Respiratory infections	3.5
Other infections	5.2
Other non infectious	4.4

(From Johnston, 1980)

- Diversity of infectious diseases in lambs



Infectious abortions

QFever, Chlam, Salmo, BD, toxo...

Waterly 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*)
 Arthritis (*E. rhusiopathia*)
 Coccidiosis
 ...

- 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

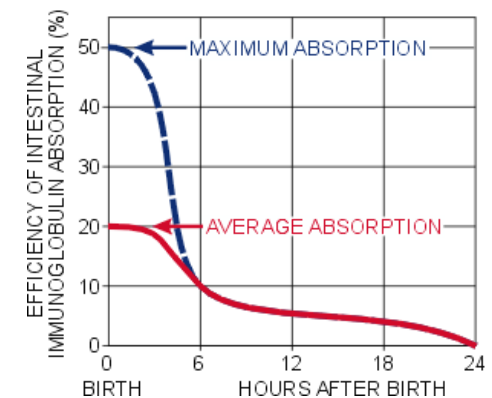
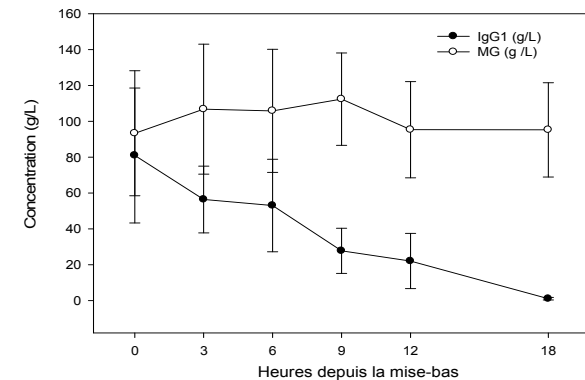
- of IgG1 absorption by epithelial cells

- Lamb vigour

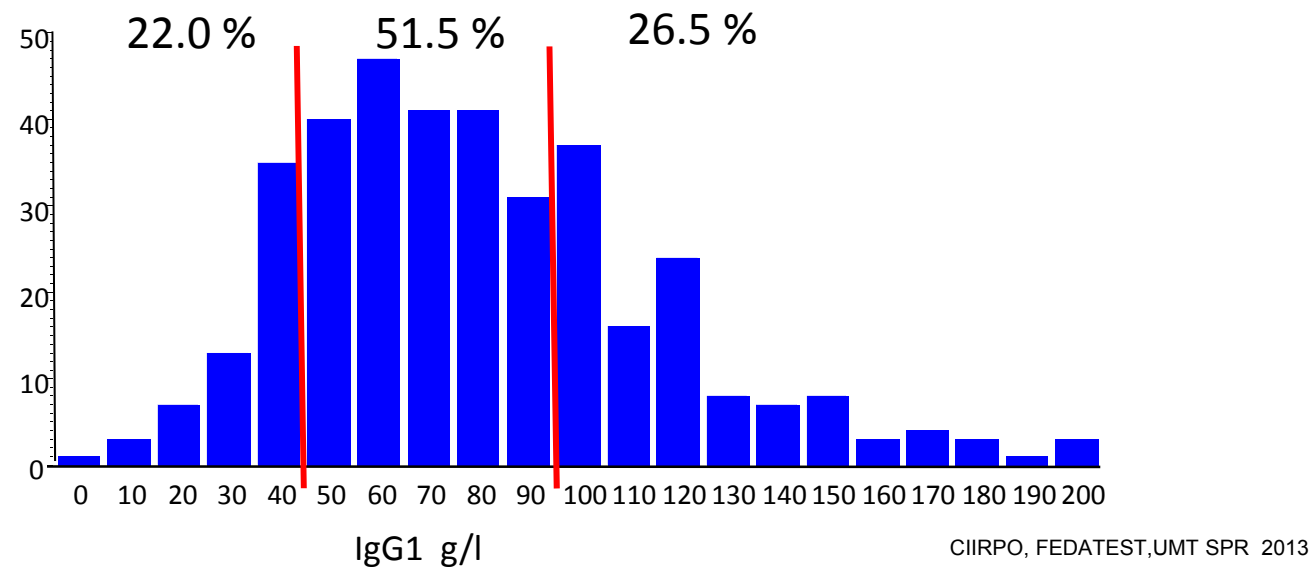
- Ewes to lamb bonding

- Genetic factors : FcRn....

- **Improve colostrum quality and quantity**



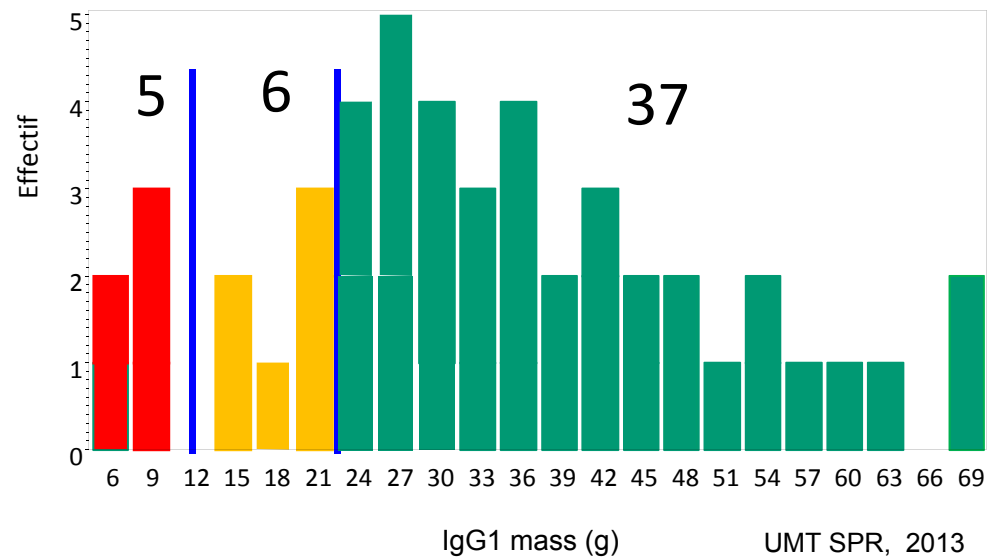
- IgG1 colostrum concentration at lambing



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

Variability of colostrum

- IgG1 mass production over 12 hours in twins lambing ewes



48 ewes : 10 % inadequate production for twins
13 % poor production for twins

- 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)
 - Effect on passive transfer of immunity : conflicting reports (Hammer et al., 2011 ; Boland et al 2005 ; Lacetera et al. 1996, 1999, 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

- High inter-racial variability, heterosis effect (Hallyday 1978, Norman 1981, Gilbert, 1988)
- 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 β 2M 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

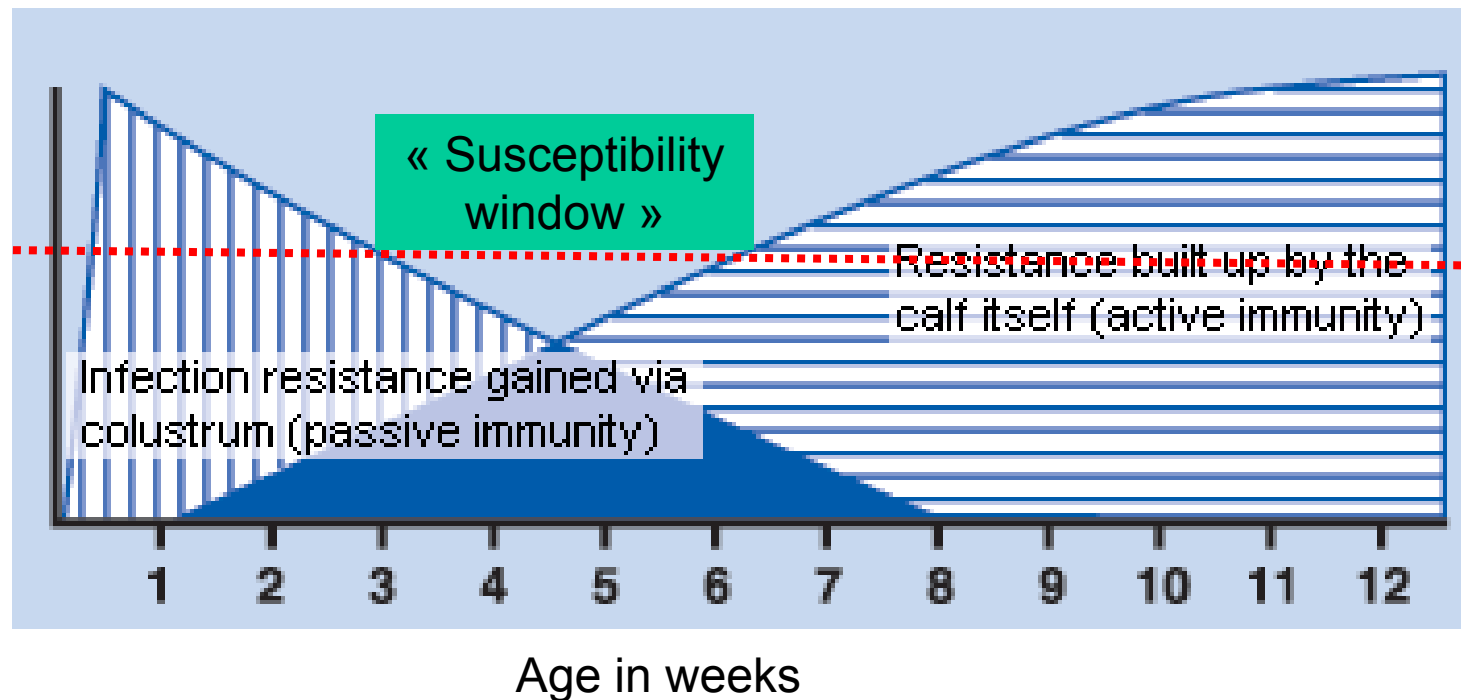


Improve immunity in lambs

- **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 \searrow IL-10 \nearrow)
 - 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 maternal 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 Oligodeoxynucleotide (CpG ODN)
 - ...
 - **Live vectors**
 - Virus, bacteria
 - **Cytokines**
 - IL-2, IFN γ , 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-IFN α 1 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
 - ...

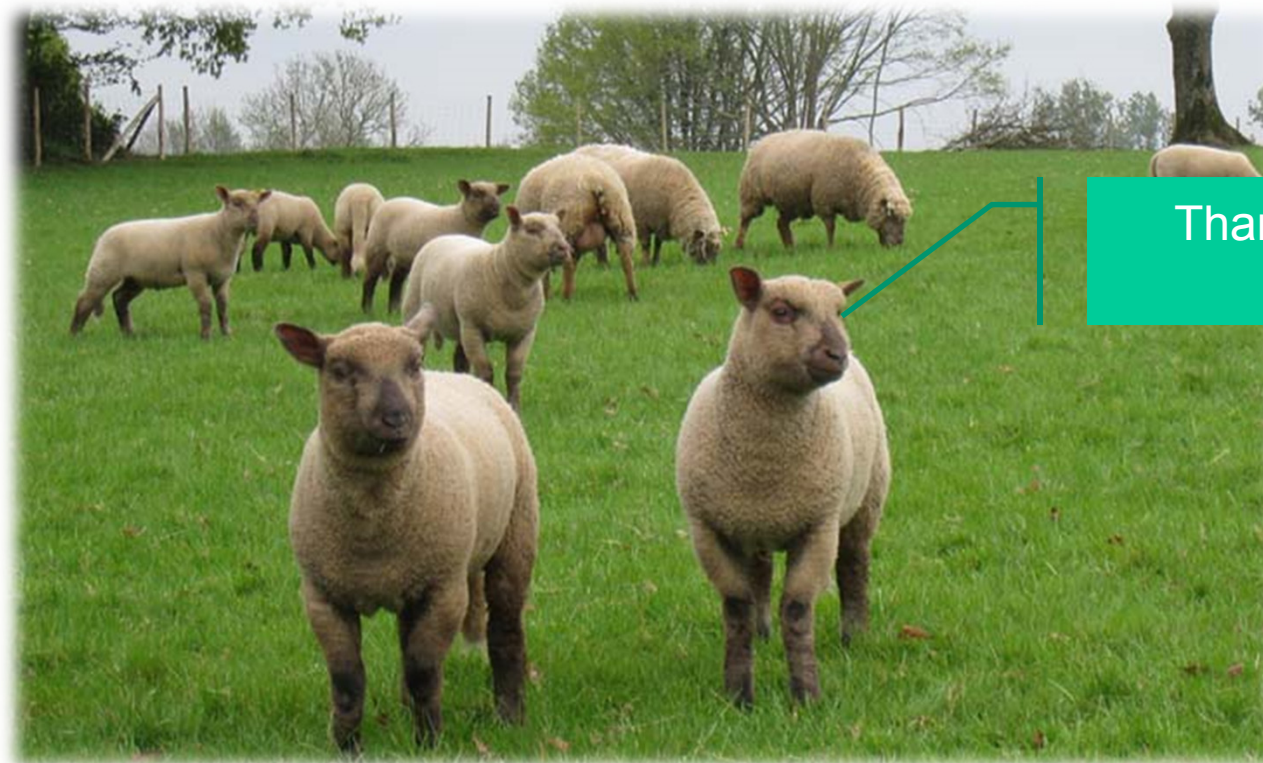
- Identification and control of risk factors
 - Improve sheepfold conception
 - Improve farmers' practices
 - ..



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