Cesarean-Derived SPF Sheep for Biomedical Research

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Animal Program Overview

- Hospital founded in 1811, first teaching affiliate of Harvard Medical School
- Mission includes Clinical Care, Teaching and Research
- **Biomedical research program**
  - Annual budget = $530M
  - 80,000 sq ft of animal facilities in 9 different locations
  - AAALAC Accreditation since 1993
  - 1000 active protocols; >350 PIs & 2000+ animals users
- **Center for Comparative Medicine**
  - Approximately 110 FTEs
  - Supports Variety of Species: Rodents, Aquatics, Rabbits, Pigs, Sheep, Dogs, Non-human Primates

Issue

- Health Status of Sheep
  - Conventional flocks
  - Appeared healthy but “not normal”
  - Diseases encountered
    - Pneumonia (chronic & acute)
    - Contagious ecthyma
    - Parasites

Problems

- Pulmonary studies
  - Baseline parameters not normal
  - Impossible to conduct experiments

- Cardiovascular studies (CHF)
  - Creation of cardiac lesion
  - Premature death related to pneumonia

- Occupational safety

Solution

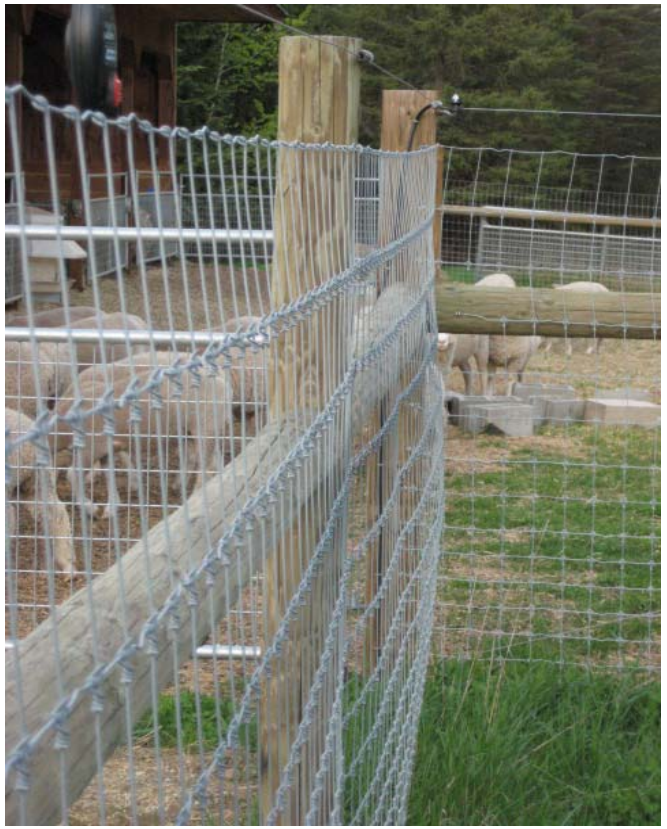
- Cesarean-derivation
- Truly closed SPF flock established
- Strict Biosecurity

Hurdles

- Housing
- Timing of surgery
- Neonatal care
- Establishment of rumen microflora
- Health monitoring (list of excluded organisms)
- Maintenance of SPF status

Housing

- Isolation from other ruminants
- Six foot perimeter fence with electric wire
- Allowed to graze
- Open 3-sided barn



Timing of Surgery

- Single Source, Polypay Breed
- Induced Estrus, Controlled Breeding
- Induced Parturition
- Timed-Caesarian Delivery
- Lambs Hand-Raised

Neonatal Care

- Within Minutes
  - Lambs isolated
  - Breathing supported
  - Body temperature maintained
- Within an Hour
  - Navel dipped
  - Heat-treated colostrum fed
  - Trained to nipple bucket with milk replacer
  - Closely monitored


SPF lambs born May 4, 2008

Establishment of Rumen Microflora

- Transfer of needed micro-organisms w/o pathogens
  - First attempt
    - Donor treated for endoparasites
    - Donor euthanatized and rumen contents collected
    - Contents centrifuged low speed
    - Each lamb received 20cc PO @ 3wks
    - Only partially successful

Establishment of Rumen Microflora

- Second attempt
  - Donor treated for endoparasites
  - Donor euthanatized and rumen removed and dipped in disinfectant
  - Brought to SPF farm and contents removed and strained through cheese cloth
  - Each lamb received 30cc orally @ 5wks

Health Monitoring

- **Bacteria**
  - *Bacteroides nodosus* (foot rot)
  - *Branhamella*
  - **Brucella*
  - **Campylobacter*
  - **Chlamydophila*
  - **Corynebacterium pseudotuberculosis*
  - **Coxiella burnetii* (Q-fever)
  - **Leptospira*
  - **Listeria monocytogenes*
  - *Mannhiemia*
  - *Mycobacterium paratuberculosis*
  - *Mycoplasma*
  - *Pasteurella*
  - **Salmonella*
- **Fungi**
  - *Ringworm

*zoonotic concern

- **Prions**
  - Scrapie
- **Protozoa**
  - **Cryptosporidia*
  - **Giardia*
  - **Toxoplasma gondii*
- **Parasites**
  - All gastrointestinal parasites (except coccidia)
  - All other helminthes, trematodes & cestodes
  - All ecto-parasites
- **Virus**
  - Bluetongue
  - Border Disease
  - Bovine Viral Diarrhea
  - *Contagious Ecthyma
  - Ovine Progressive Pneumonia

Maintenance of SPF Status

- Biosecurity
- Sentinel program
- Routine serology, microbiology, histopathology, necropsy and PCR and fecal testing
- Standard operating procedures

Results

- Neonatal survival (to weaning)
  - 2006 = 79% (59 C-sections)
  - 2007 = 80% (94 C-sections)
  - 2008 = 90% (68 C-sections)

- Percent of total mortality occurring ≤1st day
  - 2006 = 62%
  - 2007 = 50%
  - 2008 = 30%

Benefits

- Health-associated confounding research variables have been eliminated
- Truly closed source
  - no co-mingling=no disease sharing
- Animal uniformity (health and breed)
- Elimination of zoonotic disease potential

Benefits

- No quarantine period
- No “conditioning” (treatment of enzootic diseases) costs
- No “extra” animals needed to replace sick animals
- No lost time and $$ for failed or delayed experiments due to poor animal health
- No extra pen space occupied by sick or quarantined animals

Welfare Benefits

- SPF animals are spared the discomfort associated with infectious disease
- Animals are frequently handled from birth and are less fearful and more tractable
- Because of the refinement of using SPF animals, fewer animals may be required in a research project

New England Ovis, LLC

Questions?