Breeding the Problem Mare

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What is a Subfertile Mare?
AKA The “Problem” Mare

- Not pregnant after repeated matings
- Cannot carry a pregnancy to term
- Has known reproductive pathology
- Behavioral issues that affect reproduction

What Causes Subfertility?

- Breeding management
- Conformational defects
- Susceptibility to endometritis
  - Infectious endometritis
  - Post-mating induced endometritis

ALL MARES GET ENDOMETRITIS

SO WHY ARE SOME MARES DIFFERENT?

Resistant vs Susceptible Mares

Susceptible Mares

- Prior to breeding
  - Minimal inflammation
- After breeding
  - Acute inflammatory response
  - Poor ability to clear inflammation/infection
“Typical” Susceptible Mare

- Middle-aged or aged
- Pluriparous
- Pendulous uterus
  - Poor contractility
- Perineal defects

“Atypical” Susceptible Mare

- Middle-aged
- Maiden
- Cervical incompetence during estrus

Other Factors: Mucus Production

- Produced by endometrial ciliated cells
  - Protective
  - Excessive in endometritis

Other Factors: Biofilm

- Heterogenous mix of bacteria
  - Supported in extracellular matrix
  - Normal flora/protective
  - Pseudomonas spp, E. coli
- Properties of bacteria can change with conditions
  - Can result in disease
    - Dental caries
    - Antibiotic resistance

Problem Solving the Problem Mare

The “Usual” Stuff

Uterine Culture

Staphylococcus biofilm

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Uterine Cytology: Methods

- Uterine swab
- Uterine cytology brush
- Uterine biopsy

Diagnosis of *S. zooepidemicus* vs *E. coli*

- Strep infections
  - More uterine fluid
  - More positive cultures
  - More positive cytology
- *E. coli* infections
  - Low volume uterine lavage
  - RT-PCR

Interpretation of Results

- Traditional cytology
  - 5 PMN’s/hpf
  - Degenerate cells
  - Bacteria
    - *Streptococcus*
    - Fungal organisms
- Low volume lavage
  - Presence of PMN’s
  - Debris in fluid
  - Mucus strands
  - *E. coli* culture
  - Fungal culture

Low Volume Uterine Lavage: Sample Processing

400 x g for 10'

Which Method to Use for Detecting Endometritis?

- Uterine Swab Cytology
  - High rate of false negatives
- Uterine Cytology Brush
  - Higher specificity than uterine swab
- Low Volume Lavage
  - Higher sensitivity for *E. Coli* infection
- Uterine biopsy
  - More sensitive for Gram negative bacteria

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Endometrial Biopsy

Visualization of uterine lumen
Localized abnormalities of the endometrium
Visually-guided procedures
- Deep horn insemination
- Biopsy
- Laser procedures

Inflammatory cells

Hysteroscopy
- Barren mares
- Oviductal blockage
  - Plugs
  - Salpingitis
  - Adhesions
- Laparoscopic evaluation
  - Flush
  - Prostaglandin E

Oviductal Patency

Treatment Strategies

Breed Close to Ovulation
Treating the Problem Mare

The “Usual” Stuff

- **Mycobacterium phlei** cell wall extract (MCWE)
  - Settle® (Bioniche Animal Health)
  - 1.5 mg, IV or IV
  - Administered early in estrus
  - Modulates immune response
  - Both routes effective
  - Not tested combined with antibiotics

Fumoso, et al. 2007

Immunostimulants

- **Propionibacterium acnes**
  - EqStim® (Neogen Corp.)
  - Pregnancy rates improved
  - Combined with traditional treatments
    - Oxytocin
    - Antibiotics
    - Uterine lavage

Rohrbach, et al. 2007

What About Steroids?

- **Dexamethasone** (Bucca, et al. 2008)
  - 50 mg, IV
    - Within one hour of mating
    - Combined with other therapies
    - No change in pregnancy rate
    - Decreased clinical signs

- **Prednisolone** (Papa, et al. 2008)
  - 0.1 mg/kg, PO, q12h
  - 4 days starting 48h prior to mating
  - Improved pregnancy rates
  - Use with bacterial endometritis?

Immunomodulation

- Susceptible mares
  - Post-mating induced endometritis
  - Infected with *E. coli*
  - Mycobacterium cell wall extract
    - MCWE, Settle™
    - 1.5 mg, IV
  - Dexamethasone
    - 0.1 mg/kg, IV
  - Endometrial biopsies and uterine cultures
    - 3, 24, 72 h

Immunomodulation
- Pro-inflammatory cytokines (IL-1β, IL-6, IL-8)
  - Decreased with dexamethasone
- Anti-inflammatory cytokines (IL-10)
  - Increased with dexamethasone
- Serum amyloid A proteins
  - Decreased with MCWE
- Bacteria and uterine fluid
  - Decreased with both treatments
- TAKE HOME: THERE MAY BE A PLACE FOR STEROIDS IN TREATING THE MARE WITH INFLAMMATION

Mucolytics
- DMSO, kerosene
  - Chemical curettage
- N-acetylcysteine (NAC)
  - aka Mucinex®
  - Mucolytic/anti-inflammatory
  - 30 ml 20% solution
    - diluted in 150 ml saline
  - Infuse day prior to breeding
  - Oxytocin 4–6 h after infusion
  - Uterine lavage at 24 hours

Buffered Chelators
- Enhance antimicrobial activity
  - Alter cell wall
  - Paired with most antimicrobials
- Tris–EDTA
- Tricide™
  - Commercially available
    - Rood and Riddle
  - 200–500 ml/infusion
  - Lavage 12 h later

Conclusions: The Problem Mare
- Success requires attention to detail
- Patience is important!
- Use therapies wisely