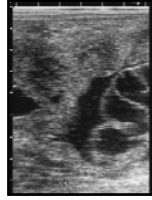


Breeding the Problem Mare



Margo L Macpherson, DVM, MS, DACT
 Malgorzata Pozor, MedVet, PhD, DACT
 Erin Runcan, DVM, DACT
 University of Florida

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

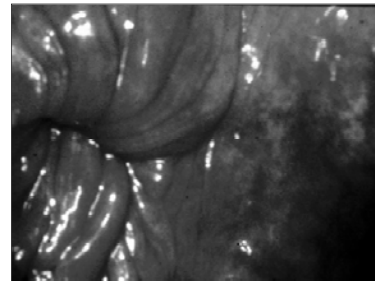


What Causes Subfertility?

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

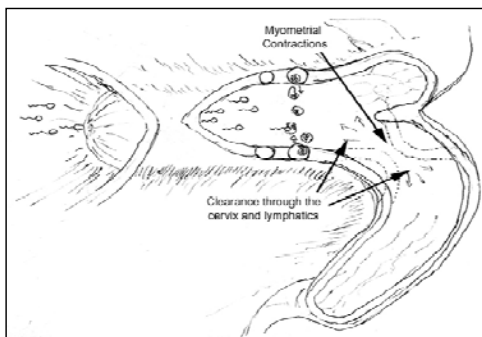


ALL MARES GET ENDOMETRITIS



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



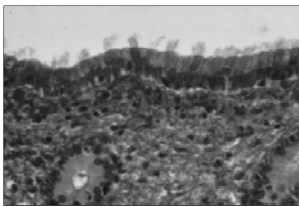
"Atypical" Susceptible Mare

- Middle-aged
- Maiden
- Cervical incompetence during estrus



Other Factors: Mucus Production

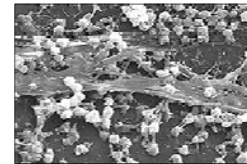
- Produced by endometrial ciliated cells
 - Protective
 - Excessive in endometritis



Causey, et al. 2000, 2008.

Other Factors: Biofilm

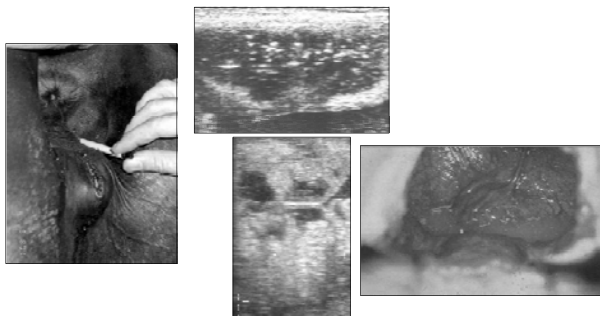
- Heterogenous mix of bacteria
 - Supported in extracellular matrix
 - Normal flora/protective
 - *Pseudomonas* spp, *E. coli*
- Properties of bacteria can change with conditions
 - Can result in disease
 - Dental caries
 - Antibiotic resistance



Staphylococcus biofilm

Problem Solving the Problem Mare

The "Usual" Stuff



Uterine Culture



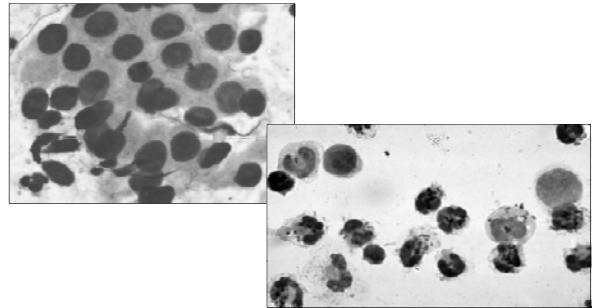
Uterine Cytology: Methods

- ▶ Uterine swab
- ▶ Uterine cytology brush
- ▶ Uterine biopsy



Nielson J. 2005

Uterine Cytology



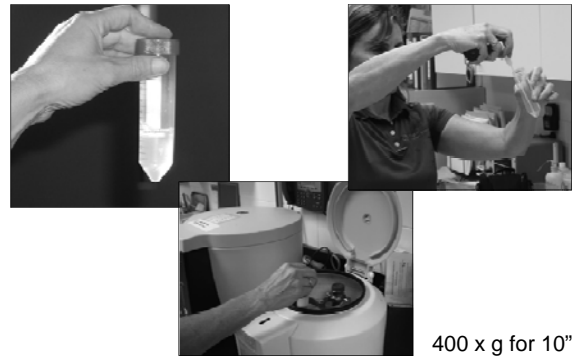
Diagnosis of *S. zooepidemicus* vs *E. coli*

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



Riddle et al, 2007; Eaton et al, 2010; Burleson et al, 2010

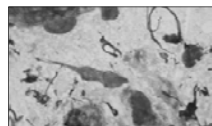
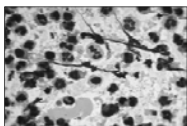
Low Volume Uterine Lavage: Sample Processing



400 x g for 10"

Intrepretation of Results

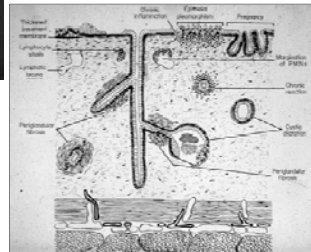
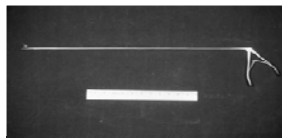
- | | |
|---|--|
| <ul style="list-style-type: none"> ▶ Traditional cytology <ul style="list-style-type: none"> ◦ 5 PMN's/hpf ◦ Degenerate cells ◦ Bacteria <ul style="list-style-type: none"> • <i>Streptococcus</i> ◦ Fungal organisms | <ul style="list-style-type: none"> ▶ Low volume lavage <ul style="list-style-type: none"> ◦ Presence of PMN's ◦ Debris in fluid ◦ Mucus strands ◦ <i>E. coli</i> culture ◦ Fungal culture |
|---|--|



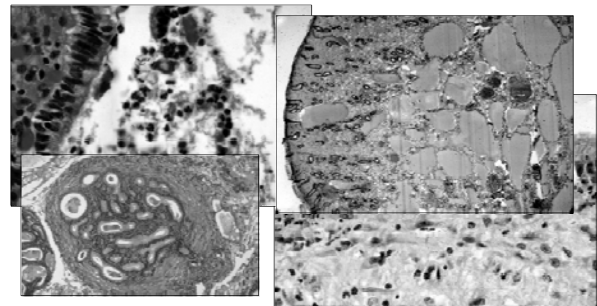
Which Method to Use for Detecting Endometritis?

- ▶ 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

Endometrial Biopsy

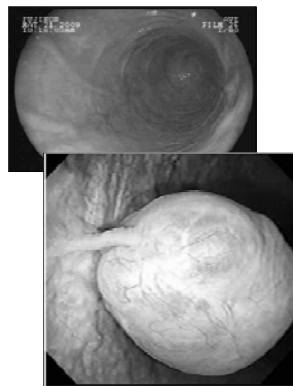


Inflammatory cells



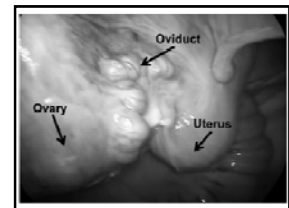
Hysteroscopy

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



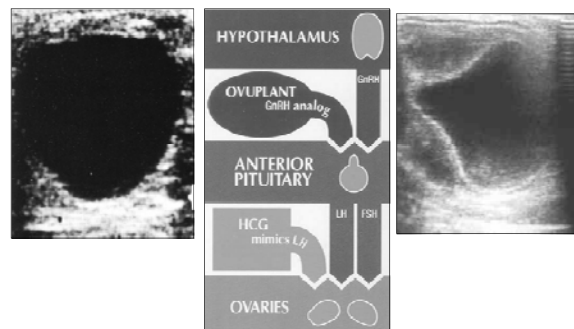
Oviductal Patency

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



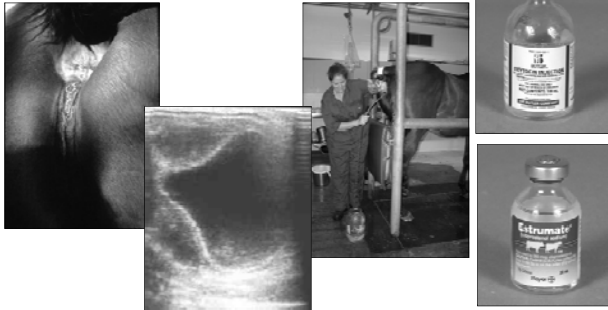
Treatment Strategies

Breed Close to Ovulation



Treating the Problem Mare

The "Usual" Stuff



Things to Use When Nothing Else Works



Immunostimulants

- ▶ *Mycobacterium phlei* cell wall extract (MCWE)
 - Settle® (Bioniche Animal Health)
 - 1.5 mg, IU 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

Christoffersen, et al. 2012, Woodward, et al. 2012

Immunomodulation

- Pro-inflammatory cytokines (IL-1 β , 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

Christoffersen, et al. 2012; Woodward, et al. 2012

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



Dascanio, 1989

Gores-Lindholm, et al. AAEP 2009.

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



Youngquist, et al. 1984; Lyle AAEP 2011

Conclusions: The Problem Mare

- Success requires attention to detail
- Patience is important!
- Use therapies wisely

