The infertile mare: What can I do?
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What defines the problem mare? Have the owners bred the mare often enough and with good quality semen to have given the mare the chance to become pregnant? Is the problem management or actual pathology? A great history and a look back at breeding management would be the first step in an investigation. Typically the mare should be bred on 3 consecutive estrous cycles with good quality semen before we would recommend an extensive workup for a reproductive problem. This requires that no issues have been identified such as post-breeding fluid accumulation, vaginal/vulvar discharges, hyperechoic edema patterns on ultrasound or others.

A complete breeding soundness examination may be warranted; however, making sure to perform a complete basic examination should not be overlooked. All too often a uterine culture is taken without a uterine cytology, providing only partial information. Most mares that have an issue with breeding should have a low volume uterine lavage for culture and cytology so as to sample the entire uterine lumen. For routine screening a uterine swab or brush may be used. Frequent ultrasound examinations may detail uterine fluid that would have been missed with every other day ultrasounds.

Endometritis – inflammation of the endometrium
Endometrosis – chronic degenerative endometritis
Metritis – inflammation of the endometrium and myometrium
Pyometra – long term purulent fluid accumulation within the uterus often accompanied by an active corpus luteum

Problem mare diagnostics: In addition to the regular aspects of palpation per rectum, ultrasound examination of the reproductive tract, a vaginal speculum examination, manual vaginal examination and uterine culture and cytology, the following tests may be considered:

1. Perform separate cultures of clitoral fossa and vagina to look for “reservoirs”
2. Do a low volume uterine lavage for culture and cytology in early estrus
3. Perform endoscopy of endometrium (hysteroscopy) to look for focal infections and other pathologies (adhesions, etc)
4. Culture through sterile speculum or “double glove” with culture swab between gloves to avoid vaginal contaminants
5. Ultrasound at 12 to 24 post treatment/insemination (earlier better) to look for delayed uterine clearance

Typically a uterine biopsy would be performed after resolution of an issue or as a means of obtaining tissue for culture or special staining. A biopsy after resolution would provide more information about the potential for the mare to form placentation capable of allowing full term support of a fetus. If the testing procedures above do not elicit a diagnosis, then more advanced diagnostics may include:
1. Culture of a uterine biopsy
2. PCR of uterine lavage solution to identify bacteria or fungal elements.
3. Special stains of a uterine biopsy such as using silver staining methods for fungal elements.

<table>
<thead>
<tr>
<th>Culture Growth</th>
<th>Neutrophils present</th>
<th>Diagnostic Determination</th>
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</thead>
<tbody>
<tr>
<td>Negative</td>
<td>Negative</td>
<td>Mare is “clean” or focal infection</td>
</tr>
<tr>
<td>Positive</td>
<td>Positive</td>
<td>Uterus is infected with pathogen isolated</td>
</tr>
<tr>
<td>Positive</td>
<td>Negative</td>
<td>Unlikely to have infected uterus; possible sample contamination; poor technique; time of cycle?; real pathogen (persistor state?)</td>
</tr>
<tr>
<td>Negative</td>
<td>Positive</td>
<td>Inflammation caused by pathogen that swabbing has missed; further diagnostics (low volume lavage, PCR, culture biopsy), focal infection, inflammation from another source</td>
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**Problem mare Therapeutics:**

1. Acetylcysteine (NAC)
   a. N-acetyl derivative of the amino acid L-cysteine
   b. Has anti-inflammatory effects (antioxidant and reduces free radicals) and mucolytic effects
   c. NAC has been shown to reduce anti-bacterial activity of aminoglycosides, fluoroquinolones & erythromycin and enhances efficacy of β-lactams against several bacterial strains.
   d. Anti-inflammatory effect: Infuse NAC (dilute 30 ml, 20% solution into 150 mL sterile saline) 24-48 hours prior to breeding. Use ecblolics 8-12 hr after infusion and/or LRS uterine lavage prior to breeding
   e. Mucolytic effect: Infuse (150 ml volume) into the uterus 24 hours prior to antimicrobial treatment, and lavage prior to antimicrobial treatment. If cloudy lavage then repeat tx.
   f. Post-breeding Tx: infuse 30 ml after breeding if post breeding lavage is cloudy or there was free fluid in uterine lumen after breeding. Give oxytocin 4-6 hr later.

2. Tricide solution treatment
   a. Potentiate antibiotics, dissolve exudate and break up biofilms
   b. Infuse 500 to 1000 ml buffered Tricide®
   c. Lavage the next day (<24 hr)
   d. If clear treat with antibiotics
   e. If cloudy or mucus strands repeat Tricide®, lavage next day. Repeat up to 2-3 x.
   f. Then treat with antibiotics for minimum of 5 days
   g. Especially for E. coli or yeast repeatedly isolated from uterus
h. Can be added to amikacin, gentamicin or clotrimazole (decreases the MIC 90 needed to kill the bacteria); also decreases MIC 90 of penicillin based drugs; tricide should **not be added** directly to ceftiofur, potassium penicillin or timentin due to precipitation of antibiotic in the solution. If these are the appropriate drugs based on culture/sensitivity, infuse tricide for 2-3 days, then intra-uterine antibiotic therapy.

3. Ceragyn
   a. 60 ml vial
   b. broad spectrum antibacterial, anti-vial and some anti-fungal properties.
   c. Causes depolarization of bacterial cell membranes and activates apoptotic pathways leading to cell death.
   d. Uterine lavage – mix 60 ml with sterile saline or LRS and use as pre or post breeding lavage (4 hr prior to or 6 to 48 hr post)
   e. Uterine infusion – infuse 60 ml into uterus for bacterial or fungal endometritis

4. bActivate
   a. Treatment with killed sperm inseminate???
   b. Reactivate latent bacteria??
   c. Product from Denmark
   d. [http://bactivate.eu/](http://bactivate.eu/)
      i. 0 hr - Do pre-activation uterine culture, place 10 ml bActivate into uterus
      ii. 24 hr later do uterine culture
      iii. 48 hr after bActivate perform antimicrobial treatment based on bacteria isolated

**Problem mare breeding**

1. Breed only once if possible
   a. Need good ovulation timing
   b. Minimize contamination

2. Choose stallion wisely
   a. Huge variation in stallion fertility

3. Choose method of breeding wisely
   a. Natural cover or Fresh AI>cooled AI>Frozen
      i. Natural cover – usually results in most potential for contamination of uterus, but semen has best longevity
      ii. **Fresh semen – Collect stallion, filter, but not cooled. Can mix with semen extender prior to insemination. Cleaner than natural cover**
      iii. Fresh cooled semen – less contamination, but longevity may be decreased from raw semen
      iv. Frozen – decreased longevity, dose and fertility
   b. Use minimum contamination breeding technique

4. Technique to inseminate may influence outcome
   a. Deep horn insemination with frozen semen to maximize dose to oviduct
b. Frozen semen equipment and method to remove semen from straws is important
   i. Direct deposition (92-96%) > Aspiration into pipette (76-87%) > Filling syringe with semen (29-79%)

**Suggested Reading List:**


