

Advanced Equine Reproduction Course

By

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The Anatomic Barriers of Defense against Endometritis in the Mare

In the mare, as well as other female mammals, three physical barriers exist between the environment and the endometrial cavity -- the vulva, vestibular sphincter, and cervix (Smith). During parturition, natural service, artificial insemination, or examination of the reproductive tract, microorganisms may penetrate the endometrial space, and are usually phagocytosed or eliminated. However, due to a variety of anatomical or physiologic function abnormalities, e.g. "wind sucking" and reduced neutrophil phagocytic capability, both pathogenic and commensal flora can initiate an inflammatory episode that departs from the normal uterine immune response. Endometritis has been classified as the least severe form of uterine infection and can be described simply as inflammation of the endometrium (Smith). Most commonly, acute endometritis is transient and the microorganisms responsible for the inflammatory reaction are removed within several estrous cycles. However, due to dysfunctional uterine immunity, some mares will tend towards persistence or recurrence of endometrial inflammation, resulting in chronic endometritis.

Bennett states that "bacterial endometritis is recognized as the most common pathologic cause of infertility in mares." Any chemical irritant or foreign protein introduction into the uterus can rapidly result in the arrival of neutrophils to the endometrium. Examples include antigenic factors, such as fungi and semen, and compounds like kerosene and DMSO (both have been suggested as successful treatments for mare subfertility). Ley indicates that in one study of 11,922 uterine cultures from a large European broodmare practice, of the 46% that demonstrated growth, the most prevalent isolates included *Escherichia coli*, B-hemolytic *Streptococcus* species, *Staphylococcus* species, *Corynebacterium* species, and other coliform bacteria. Fungal isolates seen in cultured endometrial swabs have included *Aspergillus fumigatus*, *Coccidioides immitis*, *Monosporium apiospermum*, *Candida albicans*, and several others. Clearly, when faced with a variety of etiological factors, and the effects of unresolved equine endometritis on subsequent fertility, appropriate and efficacious modes of diagnosis and therapy must be utilized. Allen describes one researcher's concern over lack of any reliable basis for selection of treatment -- especially in light of the variety of therapeutic protocols available, and their use in specific cases. I will therefore outline the methods of diagnosis and the alternative therapies used for treatment of acute equine endometritis, and include a discussion on their limitations.

Smith states that a definitive diagnosis of endometritis may be constructed from a detailed history, a complete physical examination of the mare, and appropriate laboratory procedures. Ley further details the work-up of an

endometrial infection by use of a “progressively invasive examination of the mare’s reproductive tract.” Beginning externally at the vulva, looking for purulent discharge, the clinician then performs a rectal exam to ascertain characteristics of the reproductive tract -- uterine horn size and symmetry, presence of large amounts of fluid, and other abnormalities. Transrectal ultrasonography is indicated in examination of the cervix and uterus. Next, endometrial samples should be harvested for cytology, aerobic culture, and histopathology. Pre-breeding endometrial biopsies can demonstrate a full range of histopathological changes, however, biopsies taken immediately post-resorption or abortion may provide more useful information (Allen). In fact, an endometrial biopsy can serve as the basis for predicting the ability of the endometrium to successfully support pregnancy to term (Smith). Ball et al. suggest that a low-volume uterine flush has higher yield in diagnosing endometritis based on quantitative microbiological and cytological values than the swab technique. Low-volume flushing is particularly suited to clinical evaluation of barren or subfertile mares. Any recovered isolates should then be subjected to an antimicrobial sensitivity assay, and the cytologic smear of endometrial tissue should support the clinical relevance of the bacterial or fungal isolate (evidence of inflammation). The use of multiple cultures may provide for more accurate diagnosis of uterine pathology (Waelchli et al.). The lack of any cytologic evidence of inflammation may identify bacterial isolates as procedural contaminants. Smith states as “absolute” the necessity for guarding the sampling instrument from contamination until placed within the uterine lumen. Ley indicates that the presence of more than one or two neutrophils per five microscopic fields at 400X is indicative of an active inflammatory process. Perhaps more reliably, the ratio of neutrophils to endometrial cells is also an expression of active inflammation, since it adjusts for variability in slide preparation. Fungal endometritis is diagnosed much in the same manner -- demonstration of an inflammatory reaction on cytology, and fungal elements/yeast forms on cytology or culture. Bennett discourages the use of urine cultures in aiding the diagnosis of endometritis, but indicates their use in determining microbiological etiologies once a diagnosis has been made via more classical methods. Further, intrauterine fiberoptics is suggested for imaging of lesions not made apparent through other procedures, e.g. scar tissue and endometrial cysts. Asbury states that dysfunctional uterine immunity in some mares, more commonly suspected in chronic cases of uterine infection (than in acute endometritis), may only be evident in response to challenge by a pathogen or contaminant. After spontaneous or therapy-assisted clearance of pathogens, the mare will relapse following genital examination, breeding, or foaling. It is therefore crucial that these mares are diagnosed correctly in the post-challenge period, or the success of a future full-term pregnancy is jeopardized.

Smith indicates that a number of methods of treatment for endometritis have been proposed -- surgical correction, local antibiotics, systemic antibiotics, antiseptic chemicals, uterine lavage, intrauterine plasma, and tetanus prophylaxis. Ley further points to the necessity of therapeutic combinations in some clinical cases.

Surgical correction is chosen in cases where bacterial aspiration is the result of pneumovagina, and Caslick’s vulvoplasty is most commonly performed technique. Although this temporary procedure can effectively reduce incidence of

acute endometritis in mare populations, reproductive management needs to include recognition/removal of the Caslick's prior to parturition. Administration of local antibiotics, in clinical experience, suggests restoration of near-fertility post-treatment (Smith), however, endometrial irritation can be caused by the drug/vehicle, and intrauterine antibiotic-resistant bacterial strains may be inadvertently encouraged to grow. In choosing an intraluminal antimicrobial protocol, the clinician must be aware of potential drug interactions, and have culture susceptibility results to match the drugs employed. Intrauterine antimicrobial therapy has been selected more frequently than systemic therapy by equine practitioners (Bennett, 347), although drug concentrations may be higher throughout the genital tract following systemic administration. The administration of systemic antibiotics to treat endometritis remains an empirical exercise (Ley). While systemic administration avoids multiple intrauterine infusions, and subsequent contamination, it requires more labor in medicating the mare, and higher therapy costs. Treatment of acute fungal endometritis currently does not utilize a sensitivity assay: instead, the drug protocols are selected based on a combination of clinical experience and individual mare response. Disinfectant/antiseptic intrauterine therapeutics, such as 0.5-2.0% povidone-iodine solution, can be utilized as non-specific therapy, due to their irritant nature. Ley describes an increase in uterine tone and expulsion of fluid following administration of an irritant, however, evidence of toxicity must be recognized. Uterine lavage with large volumes of warm saline is advocated for removal of accumulated fluid and debris (Smith), and is properly used in conjunction with antibiotic, antiseptic, and plasma therapy. Ley (658) chooses uterine lavage as the indicated therapy for most cases of equine endometritis, due to its ability to dilute uterine toxins, stimulate local blood flow, and increase uterine smooth muscle tone (in fact, no contraindications for its general use are presented). Intrauterine plasma infusion is thought to work as an aid to the mare's dysfunctional/hypofunctional process of bacterial opsonization (Smith). Potassium penicillin G and ticarcillin may be used in conjunctions with plasma instillation, as they do not interfere with uterine neutrophilic phagocytosis. Unfortunately, some debate exists concerning the actual efficacy of this treatment. Smith recommends consideration of tetanus antitoxin/toxoid in animals with uterine infection, as tetanus may complicate the clinical course of the disease.

Ley states that the minimum accepted treatment length for mares with acute endometritis is 3 days, with the average being 5. Post-breeding prophylactic treatment can be performed 4-6 hours after each breeding, with non-spermicidal antibiotics. Further, an opportunity exists for several days following ovulation (before the embryo arrives) to continue to clean the uterine environment, utilizing agents that increase smooth muscle tone, uterine clearance, and are not irritating (i.e. uterine lavage with warm saline). Allen details a protocol in which a deliberate mating is performed 3 days prior to expected ovulation, followed by ultrasonographic scanning of the uterus 3-12 hours later, looking for intrauterine fluid. If fluid is found, oxytocin administration and manual cervical dilation are performed, followed by intraluminal infusion of water-soluble antibiotics in mares suspected of bacterial infection/contamination.

This protocol may significantly increase conception and successful pregnancy rates in mares susceptible to infective endometritis.

Equine acute endometritis therefore can be a clinical manifestation of both mare and management faults. Both diagnostic and therapeutic modalities follow a logical progression, from demonstration of both an etiological agent and appropriate inflammatory response, to susceptibility-targeted antimicrobial administration and non-specific uterine environment therapy. To keep a brood mare in successful and acceptable reproductive performance requires recognition of acute endometritis as it occurs, willingness to systematically approach the clinical case, and motivation to prevent management and mare problems from the onset.

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