



Review Article

Equine Breeding-Induced Endometritis: A Review

Elizabeth M. Woodward PhD, Mats H. Troedsson DVM, PhD

The Maxwell H. Gluck Equine Research Center, Department of Veterinary Science, University of Kentucky, Lexington, Kentucky

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ABSTRACT

Although endometritis is a normal occurrence after breeding, persistent inflammation threatens the success of the pregnancy. Persistent endometritis has been cited as a leading reproductive health concern in the mare. A variety of factors contribute to susceptibility to persistent breeding induced endometritis, including age, endometrial quality, and reproductive history. Seminal plasma mediates the immune response to breeding, as it has protective properties for viable spermatozoa, while aiding in the recognition and targeting of dead spermatozoa by the mare's immune response. Although the adaptive immune response has been implicated in the response to breeding, the innate immune response along with mechanical clearance are the primary mechanisms suggested to act to clear endometritis. Mares susceptible to persistent breeding induced endometritis have an altered innate immune response after breeding compared to resistant mares. There are multiple tools and strategies utilized for the diagnosis and treatment of persistent endometritis. This review of the literature summarizes research investigating the causes, pathogenesis, and treatments of persistent breeding induced endometritis.

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1. Introduction

Breeding-induced endometritis is a normal physiological reaction in the horse, as it is believed that an inflammatory response is necessary for the effective removal of contaminating bacteria and excess spermatozoa introduced into the uterus [1]. In a healthy uterus, the inflammation subsides within 48 hours; however, a subset of mares fails to clear the inflammation in a timely fashion. This persistent breeding-induced endometritis (PBIE) impairs fertility and threatens the viability of the conceptus, which migrates to the uterus approximately Days 5–6 after breeding [2,3]. Hughes and Loy [4] observed a disparity in the ability to resolve uterine inflammation between young, fertile mares and older, subfertile mares after an intra-uterine challenge using *Streptococcus zooepidemicus*

infection as a model to study persistent endometritis. The authors suggested that the mares less successful in clearing uterine inflammation had an alteration in their normal uterine defense mechanism. Literature suggests that as many as 10%–15% of broodmares retain fluid 24–36 hours after breeding [5], and persistent endometritis has been cited as a leading reproductive health concern in equine veterinary practice [6].

2. Factors Contributing to Persistent Endometritis

Predisposition to persistent endometritis has been investigated and attributed (in part) to several factors. Advanced age has been associated with an altered systemic immune response in horses and other animal species, and it has been observed that age is correlated to susceptibility to persistent endometritis [5,7–9]. In addition, internal and external conformation of the reproductive organs has been associated with susceptibility to persistent endometritis. Mares with poor perineal conformation had a higher incidence of endometritis prior to

Corresponding author at: Elizabeth M. Woodward, PhD, The Maxwell H. Gluck Equine Research Center, Department of Veterinary Science, University of Kentucky, Lexington, Kentucky 40546.

E-mail address: elizabeth.woodward@uky.edu (E.M. Woodward).

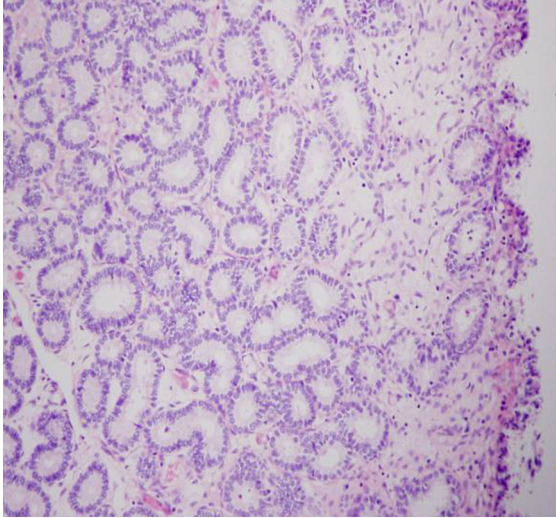


Fig. 1. Endometrial biopsy sample from a grade I mare (grading scale developed by Kenney and Doig [23]).

breeding than normal mares [10]. Furthermore, the position of the uterus within the abdominal cavity was found to be relevant in the ability to clear inflammation, when researchers found that mares less successful in clearing radiocolloid had a “pendulous” uterus dropping below the pelvic brim [11,12].

Finally, the condition of the uterus before challenge has been associated with susceptibility to persistent endometritis in several studies. Mares with excess fluid retention during diestrus were more likely to have problems with uterine fluid retention after breeding [13]. Additionally, mares with a positive uterine culture prior to breeding had lower pregnancy rates than mares with negative uterine cultures [14]. The mares in both of these studies were unable to resolve inflammation and fluid (whether it be infectious or otherwise induced).

Because persistent endometritis is diagnosed after the fact, methods to predict susceptibility to persistent endometritis are often limited to the mares’ clinical histories. Identifying mares susceptible to persistent endometritis prior to breeding to proactively treat before

the onset of persistent endometritis is important to increase the chance of a successful pregnancy. Mares have been classified as susceptible to persistent endometritis based on poor reproductive history, failure to clear inflammation induced within 96 hours after inoculation of by bacteria or spermatozoa, and endometrial pathology [15-19].

Endometrial quality has become an accepted marker of uterine health [20,21], and it has been suggested that endometrial pathologies are correlated to susceptibility to persistent infectious endometritis [16] and PBIE [19]. Poor endometrial quality has been associated with age [8] and decreased fertility [22]. A scale was developed to evaluate endometrial health based on the quality of glands and lymphatics, fibrotic changes, and infiltration of inflammatory cells [23]. An endometrial grade of I is considered normal and healthy, with active, evenly distributed uterine glands and little to no inflammatory cells (Fig. 1). In contrast, dilated glands surrounded by layers of fibrotic cells are inactive and are considered to impair function in the degenerative uterus and are assigned the most severe score of grade III (Fig. 2). To identify susceptible mares in the research setting, mares with an endometrial grade of IIB-III based on biopsy analysis have been considered “potentially susceptible” to PBIE [16-19].

3. Humoral and Cellular Immune Responses

Immunoglobulins (Ig) in the uterus were suggested to be involved with the development of persistent endometritis. Larger amounts of IgA, IgG, and IgG(T) were found in the uterine fluid of mares with impaired resistance to persistent endometritis than in normal mares [24]. A larger study found similar results with IgA levels but did not detect a difference with levels of IgG or IgG(T) [25]. Another study found that mares with positive uterine cultures had increased levels of IgA but not IgG or IgG(T) in their uterine secretions compared to that in mares with negative cultures [26]. After administering a bacterial challenge, Troedsson et al. observed a decline in uterine levels of IgG and complement C3 for the first 24 hours postchallenge (indicating a uterine response and opsonization of sperm and pathogens) in mares susceptible

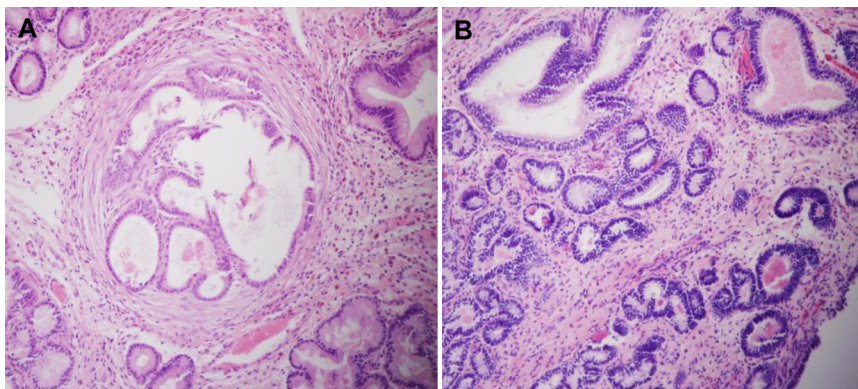


Fig. 2. Endometrial biopsy samples from a grade III mare with a fibrotic nest (A) and severe degenerative changes (B).

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