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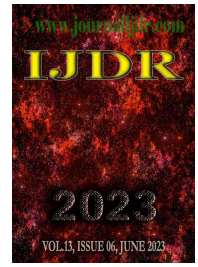
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RESEARCH ARTICLE

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BACTERIAL PATHOGENS ASSOCIATED WITH EQUINE ENDOMETRIOSIS: MECHANISMS AND PREVENTION

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ABSTRACT

Endometriosis is a severe and chronic degenerative disease commonly associated with endometritis. It is characterized by fibrosis of the endometrium and cystic dilation of endometrial glands. In mares, endometriosis is a leading cause of infertility and can result in significant economic losses in horse breeding populations. While the exact etiology of endometriosis remains multifactorial and incompletely understood, histopathological changes in the endometrium are considered as pathogenomic feature. Various bacterial strains have been implicated in causing endometritis in mares, with *Escherichia coli* being the most frequently isolated uterine bacterium. The aim of this article is to provide a comprehensive overview of endometriosis in mares, with a specific focus on the common bacterial mediators associated with the disease. Understanding the role of these bacterial mediators is crucial for the development of effective preventive, and management strategies in equine reproductive health.

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INTRODUCTION

Endometriosis is an irreversible and degenerative condition of the endometrium in mares (Hoffman *et al.*, 2009). It is characterized by periglandular fibrosis and cystic dilatation of endometrial glands, accompanied by degenerative changes in the endometrial tissue (Szóstek *et al.*, 2019). In mare, which is long-day breeder, endometriosis can disrupt the normal seasonal endocrine alterations, leading to disturbances in the cyclicity of the mare (Hoffman *et al.*, 2009). The precise etiology and mechanisms of endometriosis are not yet fully understood.

Pathophysiology: Endometriosis is most commonly observed in older mares with repeated insults to the endometrium and multiple pregnancies (Ricketts and Alonso, 1991). Under normal circumstances, uterine infections caused by bacterial invasion are cleared within five days after ovulation and conception when the fertilized oocyte reaches the uterine lumen from the oviduct (Betteridge *et al.*, 1982). The major contributing factors to the development of uterine infections include compromised uterine defense mechanisms, impaired myometrial contractility, compromised cervical drainage, and disturbed mucociliary clearance (Figure 1) (Szóstek *et al.*, 2013).

Several bacteria have been identified as causative agents of endometriosis, including *Streptococcus zooepidemicus*, *Pseudomonas aeruginosa*, *Klebsiella species*, *Escherichia coli* and *Staphylococcus capitis* (Rebordao *et al.*, 2014). Among these pathogens, *E. coli* emerges as the primary isolate associated with the activation of proinflammatory cytokines, including interleukins and TNF- α , within the endometrium (Virendra *et al.*, 2023; Christoffersen *et al.*, 2012). Altered expression of endometrial inflammatory cytokines plays a significant role in the pathogenesis and development of endometriosis (Hoffman *et al.*, 2009). Additionally, prostaglandins (Pg F_{2 α} and PgE) present an alternative pathway for fibrotic changes (Figure 2) (Oga *et al.*, 2009). Deposition of extracellular matrix by myofibroblasts, along with infiltration of mononuclear cells, triggers periglandular fibrosis (Raila, 2000). Progesterone-dependent uterine enzymes such as uteroferrin, uterocalin, and uteroglobin contribute to the cystic dilatation of endometrial glands. When coupled with bacterial invasion, this can lead to endometritis (Hoffman *et al.*, 2009). The initial histomorphological alteration associated with endometriosis involves the fibrotic differentiation of periglandular stromal cells and the centric arrangement of stromal cells around the glands (Hanada, 2014 and Schöniger, 2020). These changes lead to a reduced expression of estrogen and progesterone receptors, subsequently impacting the cyclicity of mares and increasing the risk of embryonic loss and infertility (LeBlanc, 2009 and Chu *et al.*, 2003).

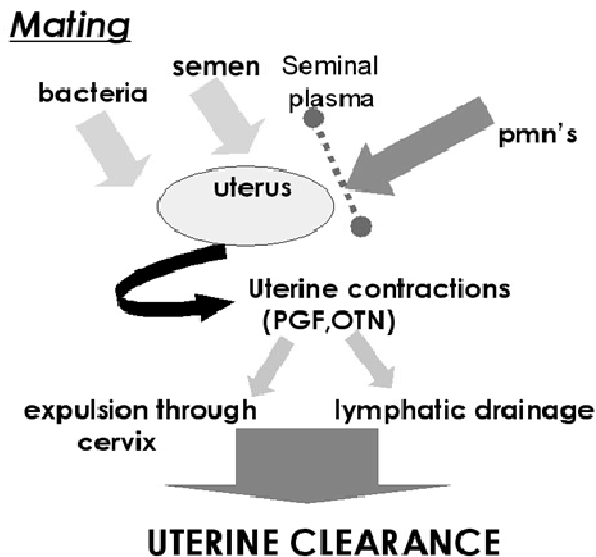


Figure 1. Normal Uterine Defense Mechanisms: Uterine Contraction, Cervical Expulsion, and Lymphatic Drainage (LSU.edu)

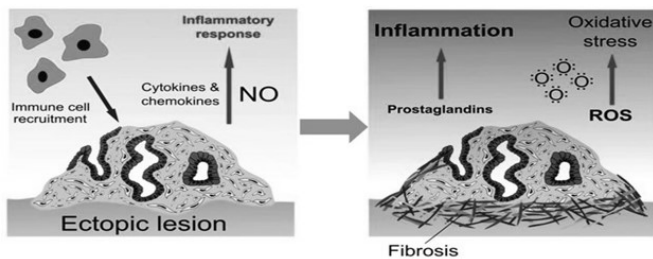


Figure 2. Mechanism of Endometriosis: Involvement of Cytokines/Chemokines and Initiation of the Inflammatory Response Pathway (Christopher et al., 2020)

Various diagnostic methods have been described in research papers and reviews, including ultrasonographic evaluation of the uterine endometrium, uterine sampling through biopsy, swab, or cytobrush techniques (Katila, 2016). Uterine biopsy is widely recognized as the gold standard diagnostic and prognostic tool for evaluating changes in the endometrium, degree of infection or inflammation, and assessing fertility in mares. This technique provides valuable insights to veterinary clinicians, enabling them to predict the likelihood of successful conception and the probability of a mare having a successful foaling (Rebordão et al., 2019).

Prevention of endometriosis: The exact cause of endometriosis remains unknown (Rebordão et al., 2014), and the changes observed in the endometrium are considered irreversible. Therefore, it is crucial to implement preventive measures to minimize the development of this condition (Aresu et al., 2005). Good breeding management practices should be followed and the administration of immunomodulators, dimethyl sulfoxide (DMSO), isotonic salt and intrauterine antibiotics may be beneficial in suspected cases, aiming to reduce the risk and severity of endometriosis in mare (Doig, 1981).

CONCLUSION

Endometriosis in mares is a chronic and challenging disease that is often accompanied by abnormal cyclicity, pregnancy failure, embryonic death and infertility. Accurate diagnosis of this condition can be achieved through the utilization of uterine biopsy techniques. Once diagnosed, veterinarians face limited treatment options for managing endometriosis. Uterine biopsy enables precise diagnosis, facilitating the implementation of preventive measures and providing valuable insights into the prognosis of future fertility and conception.

However, further studies are necessary to explore therapeutic options and develop strategies for preserving the future fertility of mares affected by this disease.

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