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Chapter 15

Endometritis and Infertility in the Mare – The Challenge in Equine Breeding Industry–A Review

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Additional information is available at the end of the chapter

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Abstract

Most major infertility problems are complex and several factors can cause failure to produce offspring. In the last few years, much of the efforts of practitioners and researchers working in equine breeding industry have been directed to individuate the pathophysiological mechanisms underlying poor reproductive performances in mares. Endometritis is on the talk in much of the recent research as the most frequent cause of subfertility in mares that cycle normally but do not conceive and in mares that cycle normally and conceive but then suffer early embryonic death. Post-breeding persistent endometritis, bacterial and other infective endometritis and poor uterine clearance have all been discussed in an attempt to define risk factors and a diagnostic algorithm. The aim of this chapter is to perform a thorough review of recent literature about endometritis. The diagnostic algorithms are carefully examined, highlighting pros as well as pitfalls of each diagnostic aid. Suggested therapeutic protocols are examined in the effort to detect what is actually recommended and what would better benefit from further corroboration. The idea that a better etiopathogenetical understanding of the endometritis remains the key to access to a correct diagnostic protocol and to a successful therapeutic plan will inspire this chapter.

Keywords: Endometritis, Mare, Diagnosis, Ultrasound, Therapy

1. Introduction

Every year many mares fail to become pregnant. These failures represent a substantial economic and genetic loss to the horse industry. Most major infertility problems are complex and several factors, singly or in combination, can cause failure to produce offspring. In the last few years, much of the efforts of practitioners and researchers working in equine breeding industry have been directed to individuate the pathophysiological mechanisms underlying poor reproductive performances in mares. To clarify, infertility includes three “problems”
mares’ types: mares that fail to cycle, mares that cycle normally but do not conceive and mares
that cycle normally and conceive but then suffer early embryonic death. Endometritis is on the
talk in much of the recent research as the most frequent cause of the last two conditions.

Post-breeding persistent endometritis, bacterial and other infective endometritis and poor
uterine clearance have all been discussed in an attempt to define risk factors and a diagnostic
algorithm, essential to reach a definitive diagnosis and to apply the appropriate therapeutic
protocol. 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 contami‐
nating bacteria and excess spermatozoa introduced into the uterus. In a healthy uterus, the
inflammation subsides within 48 hours, but the susceptible mares are not capable of resolving
the inflammation triggered by sperm and develop persistent mating-induced endometritis
(PMIE). A very strong relationship establishes between PMIE and infectious endometritis and
a complex of mare (such as age, perineal conformation, uterine clearance and cervical compe‐
tence) and microbial (such as induction of inflammation, epithelial adherence, resistance to
phagocytosis and viscosity of secretion) factors contribute to the pathogenesis of endometritis.
Traditionally, the mares that are prone to endometritis are called susceptible, in contrast to the
“resistant” ones, not prone to uterine infection.

The aim of this chapter is to perform a thorough review of recent literature about endometritis.
The cascades of inflammatory signals being complex and intertwined, the etiopathogenetical,
diagnostic and prognostic roles of the recently studied inflammatory markers are discussed.
In addition, the most common bacterial and fungal pathogens involved are reviewed, together
with the recent advances in diagnostic procedures. In fact, the diagnostic algorithms are
carefully examined, highlighting pros as well as pitfalls of each diagnostic aid. Suggested
therapeutic protocols are examined in the effort to detect what is actually recommended and
what would better benefit from further corroboration, with special attention to the correct use
of antimicrobials and antibiotics, their common way of administration and contraindications.
Consideration will be given to therapy alternatives such as proper breeding management, use
of uterine lavage, oxytocin/prostaglandin administration and treatment of the biofilm forma‐
tion. The idea that a better etiopathogenetical understanding of the endometritis remains the
key to access to a correct diagnostic protocol and to a successful therapeutic plan will inspire
this chapter.

2. Pathophysiology of endometritis in the mare

Endometritis is a major cause of infertility in the mare. It is an acute or chronic inflammation
of the endometrium that can be classified based on both its etiology and pathophysiology.
Susceptibility to persistent bacterial endometritis was characterized as early as 1969 [1]. Since
then, the physiopathological mechanisms involved in persistent endometritis and its correla‐
tion with bacterial endometritis and infertility in the mare have been discussed in several
studies [2–18]. Endometrium responds to the introduction of air, urine, semen, bacteria, fungi
or yeasts through an inflammatory reaction that ultimately hesitates in restoring an environ-
ment suitable to receive the conceptus, as it migrates from the oviduct few days after the insemination. To induce endometritis in experimental conditions, either spermatozoa or bacteria such as *Streptococcus zooepidemicus* or *Escherichia coli* are commonly infused into the uterus. A subpopulation of mares, designated as susceptible, fails to resolve the endometritis and develops a persistent inflammatory condition, which affects fertility. Furthermore, if the mare is unable to clear bacteria that may have entered the uterus during breeding, a bacterial infection can develop [19, 20].

In conclusion, any difficulty in the physical clearance of inflammatory debris from the uterus after mating or foaling triggers the endometritis. Although the mechanisms for uterine clearance for different antigens are closely related, pathophysiology, clinical signs and therapy partially differ. For these reasons, breeding-induced endometritis and bacterial endometritis will be described separately.

### 2. 1. Transient and persistent mating-induced endometritis

The transient breeding-induced endometritis is a physiological reaction in the immediate hours after breeding. It is a local inflammatory response necessary to remove excess spermatozoa and bacteria introduced into the uterus [8]. This response is limited to local inflammation, because any hematological alteration in inflammatory parameters has not yet been detected during breeding-induced endometritis [21]. Furthermore, in healthy mares, the endometritis resolves within 24–48 hours, leaving the uterus clean and free from inflammation.

#### 2. 1. 1. Mechanical clearance and inflammatory response

Semen and its extender play an important role in the induction of defense mechanisms, depending on seminal components and sperm numbers, concentration, viability and site of semen deposition. In mares mated, or artificially inseminated with fresh or cooled semen, seminal plasma activates the complement system that evokes massive migration of the polymorphonuclear leucocytes (PMNs), cytokines and mononuclear cells invasion that prepares the endometrium to receive the embryo [11, 22]. During the cryopreservation process, an important mechanism of modulation of the inflammatory response is lost due to the removal of seminal plasma, so that a severe inflammation follows the insemination with frozen/thawed semen [13]. Furthermore, seminal plasma contributes to the transport and survival of viable spermatozoa and the elimination of non-viable spermatozoa from the uterus, suppressing binding between neutrophils and viable spermatozoa [23].

The complement activation cascade led to the formation of leukotriene B4, prostaglandin (PG) E and PGF2α and other arachidonic acid metabolites, which act as chemo-attractants for PMNs in the uterus [2–5, 7]. The PMNs, on their part, drive the inflammatory response to cleaning the uterus: spermatozoa and bacteria destruction is performed by way of phagocytosis and release of neutrophil extracellular traps, composed of extensions of DNA and histones with antimicrobial action [15]. The intrauterine fluid is composed of neutrophils, inflammatory mediators and plasma proteins, including immunoglobulin and enzymes [3–4, 6–7]. The release of PGF2α stimulates myometrial contractions combined with ciliary propulsion of the


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