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Persistent uterine infection: Where to start?

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Introduction
A uterine infection can be detrimental to fertility in a number of ways; firstly, if the infection is active, the neutrophils recruited to combat the microorganisms are likely to bind and phagocytose sperm introduced during insemination thereby reducing the likelihood of conception. Secondly, persistence of a uterine infection beyond Day 6–7 after ovulation can interfere with pregnancy either by direct infection of the embryo as it enters the uterine lumen, or because the associated inflammation triggers endometrial PGF2α release leading to premature luteolysis. In the longer term, persistent or recurrent uterine infections may lead to a disturbed uterine environment, and instigate chronic degenerative changes in the endometrium that compromise the ability to maintain pregnancy; however, the evidence that recurrent infections result in chronic endometrial damage is currently lacking.

Diagnosis
In some instances, there are clear indications from a mare’s history (failure to establish pregnancy despite mating with a fertile stallion at a number of cycles; irregular cycle length) or from an initial gynaecological examination (vulval discharge; cloudy uterine fluid; excess uterine oedema) that the uterus is inflamed and/or infected. For a long time, the diagnostic cornerstone in the case of a suspected uterine infection has been the use of a guarded endometrial swab to recover a sample of uterine cells/mucus for microbiological and/or cytological examination. However, there is increasing evidence that isolated culture or cytological examination of material collected using a simple swab is not always sufficient to definitively demonstrate the presence of pathogenic microorganisms. For example, E. coli appears to stimulate a very modest neutrophil response (LeBlanc 2010), while a swab can easily be contaminated with organisms from the caudal vagina or perineum such that a positive culture alone is not definitive proof of an active endometritis; for these reasons, it is sensible to consider the results of cytology and microbiology in combination before drawing conclusions. Even then, small volume uterine lavage and uterine biopsy both appear to deliver material that is more sensitive and specific in the diagnosis of uterine infection.

Indeed, there is a growing body of opinion that some microorganisms are able to avoid diagnosis during initial sampling using a guarded swab. Organisms suspected to be capable of evading detection by swabbing include fungi/yeasts, which can exist as an endometrial biofilm, or because the associated inflammation triggers endometrial PGF2α release leading to premature luteolysis. In the absence of a suitable endoscope, ultrasonographic examination of a fluid-filled uterus can help identify adhesions, as strands spanning the lumen or failure of a horn to fill normally.

If and when underlying abnormalities have been addressed, mares with recurrent problems will require frequent monitoring and early and aggressive treatment (ecbolics, uterine lavage) of any problems surfacing in the period around insemination. There is also increasing evidence that strategic use of immunomodulators, in particular corticosteroids, may normalise the disturbed uterine inflammatory response thought to underlie heightened susceptibility to PMIE.

Conclusions
Persistent uterine infections are relatively uncommon problem in broodmares but, when they do occur, present a considerable diagnostic and therapeutic challenge. There is increasing speculation that endometrial swabbing may fail to identify some organisms because they are somehow either localised or sequestered within the uterus (e.g. deep in the endometrium, dormant, in biofilms, partially walled off). Small volume lavage may improve sensitivity of detection by sampling from the entire uterus, while a biopsy allows examination of the deeper layers of the endometrium and may give useful additional information about degenerative changes. Initial manipulations can also trigger a response that facilitates successful detection of an infection 1–2 days later. In recalcitrant cases, however, a more thorough examination of the entire genital tract, and for coincidental endocrinological abnormalities (e.g. pituitary pars intermedia dysfunction), is warranted to uncover and allow correction of any predisposing factors.

References