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Review

Contagious equine metritis: Artificial reproduction changes the epidemiologic paradigm

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ABSTRACT

Recent CEM outbreak reports reflect a novel epidemiologic manifestation with a markedly different risk association for transmission via artificial reproduction and subsequent to inadvertent importation of unapparent carrier stallions. Artificial breeding has an increased association with horizontal or fomite-associated transmission. Reported risk factors include inadequate biosecurity protocols at centralised breeding facilities associated with stallion management and methods of semen collection, processing and transport. Detection of carriers is based on traditional bacteriology from genital swabs and despite limitations inherent to *Taylorella equigenitalis* is currently the gold standard applied in all international trade and movement protocols. These limitations are reported to be overcome by PCR assays improving diagnostic sensitivity and specificity, practicality, turn-around times, through-put and cost efficacy. Molecular methods have increased understanding of the *Taylorelleae*, facilitate epidemiologic surveillance and outbreak control strategies. Validation and international regulatory acceptance of a robust PCR-based assay and the undefined risks in association with cryopreserved semen and embryos are future areas warranting further investigation.

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1. Introduction

1.1. Historical context

A previously unknown sexually-transmitted disease causing subfertility in the Thoroughbred mare population of Newmarket, United Kingdom was reported during the 1977 Thoroughbred breeding season (Crowhurst, 1977; Platt et al., 1977: Timoney et al., 1977). The origin of this extremely contagious non-systemic disease manifestation was suspected to be via introduction of mares from Ireland for breeding by Newmarket stallions following an earlier shipment of Thoroughbred mares from France to Ireland in 1976 (Eaglesome and Garcia, 1979; Luddy and Kutzler, 2010). This disease manifestation due to a hitherto unknown micro-organism is characterised by shortened inter-oestrus intervals and poor pregnancy rates associated with a muco-purulent vulvar discharge and was termed "contagious equine metritis" (CEM). The aetiologic organism was subsequently established as a bacterium, initially described as Haemophilis equigenitalis by Taylor et al. (1978) but later renamed as Taylorella equigenitalis (IJSB, 1984; Timoney, 2011). The disease was recognised and reported within a short interval from Ireland, Australia and Belgium. Despite the rapid imposition of a ban on the importation of horses into the USA and Canada from the United Kingdom, Ireland and France, CEM was confirmed in Kentucky (USA) and France in 1978, the latter outbreak included non-Thoroughbred horses, and in 1979 in Missouri (USA) and Germany. Thereafter, having achieving the status of being amongst the most regulated equine diseases internationally, it has become established or reported as sporadic epizootics in various countries, most recently South Africa (2011) and the United Kingdom (2012). There is probably a greater global distribution than is currently reported. The current assumption is that the episodic "source of contagion" is often mainland Europe, probably due to the endemic status within the resident non-Thoroughbreds populations. CEM has been confirmed from at least 30 countries in Europe, North and South America, Japan, Australia and South Africa (Timoney et al., 1977; Swerczek, 1978; Timoney, 2007; Erdman et al., 2011; Timoney, 2011; DEFRA, 2012; May et al., 2012; Ricketts et al., 2012).

1.2. CEM emerges as a classical venereal disease of horses

CEM is recognised as a true venereal disease associated with the introduction of *T. equigenitalis* during natural breeding by carrier stallions or via artificial breeding with contaminated semen obtained from carrier stallions. The resultant endometritis in the acutely-infected mare is manifested by a vulvar discharge and an irregular return to oestrus as a consequence of conception failure or early embryonic death, and subsequent need for her to be rebred. The role of unapparent carrier animals, both stallions and mares is central to the pathogenesis, dissemination and persistence as a smegma-associated colonist of the external genitalia. Reports detail an adverse, albeit temporary, effect on mare fertility, generally insidious in nature, but profound particularly in naïve populations. This has classically resulted in considerable

economic losses and impacted negatively on breeding management and reproductive outcomes in natural, particularly, Thoroughbred breeding systems (Luddy and Kutzler, 2010; Timoney, 2011). The regulatory restrictions associated with CEM have and continue to limit freedom of movement and trade of horses, which affects Thoroughbred and other breeding industries. The associated costs of quarantine and surveillance measures and those accrued by outbreak management and treatment protocols in countries where the disease is regulated are difficult to quantify (Powell, 1978; Eaglesome and Garcia, 1979; Luddy and Kutzler, 2010; Erdman et al., 2011; Timoney, 2011).

1.3. CEM as a re-emergent disease associated with artificial breeding populations

The most recent reports reflect a developing trend for an association of CEM outbreaks with artificial breeding. This is in contrast with the previously reported outbreaks that primarily affected Thoroughbred breeding. The increased application of these methods, particularly artificial insemination (AI) in non-Thoroughbreds globally has greatly increased the risk for an isolated source to widely disseminate the disease and added to this, are those risks associated with the cross-boundary translocation of a carrier animal (Timoney, 2007). The current ubiquitous shipping of chilled semen in particular and the transfer and indefinite storage of cryopreserved semen both domestically and internationally are important in potential dispersal of contagion both geographically and temporally. The potential for transmission is exacerbated by the poorly defined risks associated with transported semen, particularly cryopreserved semen and embryos. The current epidemiology frequently describes various forms of horizontal and non-coital spread of contagion. This is associated with multiple potential fomites due to semen collection, processing and storage for fresh, chilled or cryopreserved usage. This is also consequent to inadequate biosecurity. The role of centralised breeding centres in the spread of this disease is common to several reports (Kristula and Smith, 2004; Timoney, 2007, 2011; Luddy and Kutzler, 2010; Aalsburg and Erdman, 2011; Erdman et al., 2011; May et al., 2012; Ricketts et al., 2012). At these centres, large numbers of stallions are transferred for semen collection facilitating direct and indirect contact between stallions, following which their subsequent dispersal to their farms of origin promote disease transmission. The direct impacts on economic and breeding performance in non-Thoroughbreds are undefined.

The classical manifestation as an emergent venereal disease affecting Thoroughbreds worldwide has essentially disappeared subsequent to almost four decades of international regulation and disease surveillance. This review will focus on the most recent information reporting on an altered epidemiological manifestation of an already well-recognised infectious disease threat that is currently associated with non-Thoroughbred horse breeds and artificial reproduction. The aim is to revisit the traditionally-accepted understanding of CEM to address the novel and emergent risks associated with artificial breeding

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