

Evidence-based Clinical Question

Does early antibiotic use in horses with 'strangles' cause metastatic *Streptococcus equi* bacterial infections?

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This issue of *EVE* introduces a monthly column looking at a clinically relevant question and evaluating it from an evidence-based point of view. Contributions from readers are welcomed. Please send 800–1000 word articles to David Ramey, DVM, ponydoc@pacbell.net

Streptococcus equi (*Streptococcus equi* ssp. *equi*) is a Lancefield group C *Streptococcus* that causes 'strangles', a highly contagious purulent lymphadenitis and pharyngitis of members of the family *Equidae*. In most cases, *S. equi* infection in horses causes a transient lymphadenopathy of the mandibular and retropharyngeal lymph nodes, with subsequent abscessation (Foreman 1999; Sweeney *et al.* 2005). Although the disease is associated with significant morbidity, most infected horses ultimately recover. However, in some cases, metastatic dissemination develops. This is sometimes referred to as 'bastard strangles,' a perhaps unfortunate and archaic term that has become embedded in the veterinary literature, first having appeared in the early 19th century (Slater 2003). Spread of the *S. equi* organism has been reported to many organs and tissues of the horse's body, including, but not limited to, the lungs, mesentery, liver, and brain (Ford and Lokai 1980; Spoormakers *et al.* 2003). There appears to be a belief, and some authors have stated, that the institution of antimicrobial therapy in the treatment of *S. equi* infections of horses is contraindicated prior to maturation of the submandibular abscesses that are typical of the clinical course of the disease, as the use of such therapy may enhance the frequency of multifocal abscesses (Beech 1979).

The reason(s) for concerns about antibiotics are speculative. Early observers rather accurately, if colourfully, described the pathobiology of metastatic abscessation: "... for want of properly effecting suppuration, the humours frequently settle, or are translated to the lungs, the fleshy bowels or falling on the fleshy part of the hindquarters ... which sometimes kill the horse..." (Bartlett 1777). It has more recently been suggested that antibiotics such as procaine penicillin G may somehow affect the bacterium in such a way as to result in an inadequate host immune response (Bryans and Moore 1972; Beech 1979; Clabough and Scrutchfield 1987; Sweeney 1987; Timoney 1993; Semrad 1999). For example, one such hypothesis

suggests that antibiotics alter bacterial protein synthesis, thereby reducing immunogen levels, resulting in a suboptimal immune response, thereby allowing for dissemination of the bacterium (Sweeney *et al.* 2005). Alternatively, another hypothesis is that, since penicillin works on the bacterial cell wall, it somehow prevents the horse from developing immunity, allowing for spread of the infection (Beech 1979).

However, and perhaps remarkably so, given the persistence of the belief in the veterinary literature, there appears to be no clinical or experimental evidence to support the supposition that treatment with antimicrobial agents at any stage in the course of the clinical disease 'strangles' increases the prevalence of metastatic dissemination of the organism. One of the first references suggesting that increased incidence of disseminated *S. equi* infections were associated with antimicrobial therapy appears to come from a publication on streptococcal disease in human medicine, in which 2 veterinary authors gave their 'clinical observations' of such an association in horses (Foreman 1999; Sweeney *et al.* 2005). These observations appear to have been perpetuated in subsequent publications.

There appear to be no prospective studies comparing horses treated with antimicrobials to untreated horses. Even the prevalence of 'bastard strangles' is unknown. In 4 cases of horses suffering from cerebral damage due to metastatic *S. equi* abscesses, confirmed *antemortem* by MRI, and by *post mortem* examination, no antibiotics were used in any of the cases before neurological complications were identified (Spoormakers *et al.* 2003). Perhaps paradoxically, and particularly so given the concerns about antibiotics in the treatment of strangles, long-term (2–6 month) antimicrobial therapy with procaine penicillin G has resulted in clinical resolution of internal abscesses in many animals (Rumbaugh 1978).

Quality of evidence

The level of evidence supporting the contention that early antibiotic use in horses with 'strangles' causes metastatic *S. equi* bacterial infection is the lowest level of evidence, level 5: as described by the Oxford-based Centre for Evidence-Based Medicine (Anon 2007). That is, the available evidence is that

of an expert opinion without explicit critical appraisal. Otherwise stated, there is no strong evidence to support the contention, and such evidence as exists is essentially unsupported anecdote.

Clinical implications

In the treatment of horses clinically affected with 'strangles,' antibiotics may or may not be indicated at various stages of the disease. Firm evidence supporting and 'optimum' timing of the use of antibiotics in the treatment of strangles does not exist. In addition, actual data supporting an association between the use of antibiotics and the development of disseminated *S. equi* infection does not exist.

If questions regarding any potential relationship between the use of antibiotics and the occurrence of disseminated *S. equi* abscesses in horses are to be answered, future research should be focused on prospective studies. Useful strategies to improve the quality of the evidence available would include prospective matched-pair trials.

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