New Perspectives for the Diagnosis, Control, Treatment, and Prevention of Strangles in Horses

Andrew S. Waller, BSc, PhD

KEYWORDS

• Strangles • *Streptococcus equi* • ELISA • qPCR • Vaccine

KEY POINTS

- The ability of *Streptococcus equi* to establish persistent infection, usually within the guttural pouches, is critical to interepizootic transmission, the recurrence of strangles, and the high incidence of this disease around the world.
- The lack of clinical signs shown by persistently infected carriers emphasizes the need to implement effective quarantine and testing procedures for their identification and treatment before they come into contact with an existing herd.
- A blood sample taken on arrival can be tested to identify horses that may have been recently exposed to, or are persistently infected with, *S equi*, and that require further investigation.
- Quantitative polymerase chain reaction tests for *S equi* are now regarded as the gold standard for the detection of *S equi*.
- The development of effective vaccines against strangles that permit the differentiation of infected from vaccinated animals remains a significant unmet objective.

INTRODUCTION

Strangles was first reported in 1251 by Jordanus Ruffus,[1] an officer in the imperial court of Emperor Frederick II, although the disease almost certainly has older origins. Despite improvements in the health and management of horse populations, strangles remains the most frequently diagnosed infectious disease of horses worldwide. Only

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Centre for Preventive Medicine, Animal Health Trust, Lanwades Park, Kentford, Newmarket, Suffolk CB8 7UU, UK
E-mail address: andrew.waller@aht.org.uk

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the geographically isolated Icelandic horse population remains free of strangles, a situation that has been maintained through a virtual absence of horse imports for more than 1000 years. In excess of 600 outbreaks of strangles are estimated to occur in the United Kingdom alone each year.[2] Outbreaks can involve all of the horses on a yard, require movement restrictions that often remain in force for more than 2 months, and incur an economic cost to some premises that may exceed £250,000 ($425,000).

THE CAUSAL AGENT

Strangles is caused by infection with *Streptococcus equi* subspecies *equi* (*S equi*), which, despite the inference from its name, is a subgroup of the diverse population of *S equi* subspecies *zooepidemicus* (*Streptococcus zooepidemicus*), with which it shares more than 97% DNA identity.[3] Nonequine infections with *S zooepidemicus* can be severe, including cases of acute fatal hemorrhagic pneumonia in dogs,[4–6] and septicemia, meningitis, and toxic shock syndrome in humans.[7–10] However, despite its ability to cause severe clinical signs and its close relationship with *S equi*, *S zooepidemicus* is often regarded as a commensal organism of the equine upper respiratory tract. *S zooepidemicus* is associated with a variety of diseases in horses, including uterine infections of mares[11,12] and ulcerative keratitis.[13] Investigations of outbreaks of respiratory disease caused by *S zooepidemicus* have been confounded by the diversity of this group of bacteria and the ability of outbreak strains to persistently infect the tonsils of recovered horses.[14] Emerging evidence supports epidemiologic studies that suggested a causal role for *S zooepidemicus* in cases of respiratory disease,[15] and modern typing methods[16] have directly linked specific strains to individual outbreaks.[17,18] Such data indicate that the population of *S zooepidemicus* that is resident in the tonsils of horses includes pathogenic strains and provides a snapshot of the history of infection within an individual animal.[19] The differentiation of *S equi* from the resident population of *S zooepidemicus* and the immune responses to these closely related pathogens is a particular challenge for modern diagnostic techniques and is described in more detail later.

CLINICAL SIGNS OF STRANGLES

Strangles is characterized by pyrexia, followed by abscessation of lymph nodes in the head and neck.[20] The name strangles was coined from the signs of dysphagia that some horses experience. Some of these horses are suffocated by the enlarged lymph nodes, which can obstruct the airway. Affected animals develop pharyngitis, which may lead to them being reluctant to eat, particularly dried food, resulting in anorexia. Some affected horses stand with their necks extended and depression is common.

Following entry of *S equi* via the nose or mouth, the organism attaches to and invades the tonsillar crypts of the oropharynx and nasopharynx and can be detected in the lymph nodes of the head and neck within 3 hours after infection.[21] The transient attachment of *S equi* to the oropharynx and nasopharynx before invasion into adjacent lymphoid tissue is highlighted by an inability to detect *S equi* using nasopharyngeal swabs or washes taken 24 hours after infection. Clusters of *S equi* are apparent in the lamina propria after 48 hours.[21] Superantigens,[22,23] phospholipase A_2 toxins,[3] streptolysin S,[24] and several other surface and secreted proteins[25–29] produced by *S equi* modulate the proliferation and activity of neutrophils, leading to a failure of innate immune defences.[21] For example, the SeM surface protein is known to bind fibrinogen and immunoglobulin, providing an increased resistance to phagocytosis.[25,30–34]