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“STRANGLIES” - WHAT IS THE LATEST INFORMATION?

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Introduction

“Strangles” is an infectious, highly contagious disease of the upper respiratory tract of horses which was first described in the veterinary literature by Jordanus Rufus in 1251. Despite the length of time this disease had been investigated, its epidemiology, diagnosis, treatment and control have been problematic for horse industries worldwide. However, recent advances in our knowledge of this disease, particularly regarding the source of infection, diagnosis and vaccination have allowed significant progress to be made for this important equine disease.

Causative agent

“Strangles” is caused by the bacterium Streptococcus equi subsp equi. Recent investigations have demonstrated that it is derived from another closely related bacteria, S equi subsp zoopneumonia as a genovar or biovar1. The terminology used in this paper to describe these 2 bacteria will be simplified to S equi and S zoopneumonia respectively. S zoopneumonia is part of the normal flora of mucous membranes of horses, including the upper respiratory tract. In comparison, S equi is not considered part of the normal flora but may be found on mucous membranes of the upper respiratory tract of carrier animals.

Epidemiology

The source of infection in outbreaks of strangles is variable but frequently involves purulent discharges from horses with active and recovering infections. The subsequent transmission to naïve horses may be either direct, through nose-to-nose contact, or indirect, through sharing of contaminated housing, water, feed, or equipment. In addition, humans such as handlers, farriers and veterinarians may act as fomites for transmission. Another source of infection that has become increasing recognised are apparently healthy horses recovering from a recent infection which may continue to harbour the organism and transmit to in-contact naïve horses via nasal secretions2.

Environmental persistence of the bacteria is not well understood, especially under field conditions. Laboratory studies1 have shown the organism may survive on wood at 2°C for 63 days and for 48 days on glass or wood at 20°C. However, these studies did not take into account competing bacterial flora or other environmental confounding factors.

Pathogenesis

S. equi enters via the mouth or nose after ingestion or inhalation. The number of bacteria required to cause invasion and disease (infectious dose) is not known under natural conditions, but > 106 cfu's are required using experimental transmission. Once inhaled/ingested, S equi attaches to mucosal cells lining the lingual, palatine, pharyngeal and tubal tonsils. Attachment is mediated via surface exposed proteins, but no colonisation occurs at these sites. Direct invasion of the mucosa and subsequent translocation to the mandibular and suprapharyngeal lymph nodes that drain the pharyngeal and tonsillar regions occurs within hours of transmission.

Gram positive organisms, including S equi, contain a large amount of peptidoglycan in their outer cell walls. This molecule interacts with the host's defence molecules, including complement, to induce powerful chemotactic factors that attract large numbers of neutrophils to the site of infection. Although these cells are the first line of defence against many (non-pathogenic) bacteria, they fail to phagocytose and kill S equi due to the presence of a range of anti-phagocytic molecules including an hyaluronic acid capsule, SeM protein and Mac protein. The result is an accumulation of many extracellular S equi in long chains surrounded by large numbers of degenerating neutrophils and cellular debris, but gross evidence of abscessation is usually not visible until 3-5 days post infection. The enzymes Streptolysin S and streptokinase may further contribute to abscess development by damaging cell membranes causing lysis of neutrophils1. At this stage, abscess development is rapid and is often accompanied by lymph...
accumulation in afferent lymphatics. The host attempts to contain the growing abscess through development of a fibrous tissue capsule, which thickens over time.

S equi is eventually cleared by a combination of lysis of the abscess capsule and evacuation of its contents, and development of acquired immunity. Strong antibody (Ab) responses to a variety of surface exposed proteins, including SeM, are produced by convalescent horses and include serum IgGb and IgGa, and mucosal IgA and IgGb3. These immunoglobulins induce opsonisation of the bacteria with subsequent phagocytosis and clearing. Horses in the immediate convalescent period are resistant to challenge with higher numbers of organisms, but a small % of these horses may become re-infected within several months, probably due to a failure to produce or maintain an adequate concentration of the relevant mucosal and systemic antibodies1. Approximately 75% of horses develop a solid, enduring immunity after recovery from disease which persists for 5 years or longer1. These older horses with residual immunity have limited susceptibility and may develop a mild form of stangles (often termed “catarrhal stangles”). However, these horses may shed virulent S equi that will produce severe disease in naïve, younger horses.

Milk from mares that have recovered from strangles contains IgGb and IgA with specificities similar to those found in nasopharyngeal mucus of convalescent horses3 and which usually confer maternal immunity to suckling foals until weaning. Colostral antibodies ingested during the first 24 hours of life also will re-circulate to the nasopharyngeal mucosa, providing an additional source of protection1.

**Clinical signs**

A characteristic feature of “strangles” is the abrupt onset of fever, with rectal temperatures of 103°F or higher. This occurs between 3 and 14 days after exposure and is associated with release of pyrogens. Fever is the first clinical signs observed and persists as lymphadenopathy develops and abscesses mature. Nasal shedding of S equi usually begins 2 - 3 days after onset of fever and persists for 2 - 3 weeks in most animals. However, some animals never shed whilst others shed for prolonged periods (see Carriers).

Other clinical signs in the early stages of infection may include dysphagia and anorexia due to pharyngitis, laryngitis and rhinitis. Affected horses are often reluctant to eat and may stand with the necks extended to ease the pain. Nasal reflux may occur during this phase after trying to swallow food or water. Horses may also be listless with signs of depression. Bilateral nasal discharge is usually present, which is initially serous then rapidly becomes mucopurulent to purulent, profuse and tenacious. Accumulation of purulent exudates may cause snuffling or rattling of the upper respiratory noise. The nasal and ocular mucous membranes may be hyperaemic and ocular nasal discharge is observed in some horses, which may contain S equi.

Acute swelling of lymph nodes (LNs) is a major clinical feature. This swelling represents abscess formation which can become so large as to obstruct the upper airways (hence the name “strangles”). The submandibular and retropharyngeal LNs are equally involved, with swelling that is clinically evident usually around 1 week after infection. The first signs of lymphadenopathy is frequently hot, diffuse, painful oedema around the site of the infected lymph node. Serum may ooze through the overlying skin as abscesses mature and enlarge, before they rupture to drain tenacious, creamy, non-malodorous pus. However, deeper abscesses may take several days to weeks to develop external drainage. In the meantime, the swelling may exert pressure on the pharynx, larynx, trachea and oesophagus resulting in severe dyspnoea, stridor, dysphagia and in some severe cases competitive respiratory obstruction requiring tracheostomy. Squeezing of the larynx in these horses may elicit marked pain and gagging. Abscessation of retropharyngeal LNs is not always appreciable externally and these may drain internally causing empyema of the guttural pouch. In these cases, large quantities of pus may drain from the mouth or nose. Other lymph nodes of the rostral neck (parotid, cranial cervical) may become involved and abscessate. Periorbital abscesses may cause marked swelling of the eyelids.

Coughing is not a significant feature of this disease, helping differentiation from other infectious causes of upper respiratory tract disease. However, some horses do produce a soft, moist cough that may become productive as disease worsens.

A number of clinicopathological changes may be observed in horses with strangles and include moderate
to marked leucocytosis due to a mature neutrophilia, and elevated serum protein due to hyperfibrinogenaemia and hyperglobulinaemia. Horses with metastatic spread (see Complications) may also have anaemia of chronic disease, and additional changes in biochemical analytes reflecting the site of spread.

Severity of disease in affected horses varies greatly and depends on challenge load (numbers of bacteria), strain of bacteria and immune status of the horse. Older horses often exhibit a mild form of the disease characterized by nasal discharge, small abscesses, and rapid resolution of disease. In contrast, younger horses are more likely to develop severe lymph node abscessation that subsequently opens and drains.

**Carrier horses**

Apparently healthy horses recovering from disease can continue to harbour *S equi* for several weeks after clinical signs have disappeared. However, the organism cannot be isolated from the majority of horses 4 to 6 weeks after total recovery2. Therefore a recovered horse may be a potential source of infection for at least 6 weeks after clinical signs have resolved.

Although most horses are capable of complete recovery from infection, a small % of horses continue to harbour *S equi* for prolonged periods with periodic shedding of the organism. These long-term, subclinical carriers are an important source of infection for naïve, susceptible animals and help maintain the organism within a herd. Furthermore, their introduction to new farms may be a source of outbreaks, even under well-managed conditions. These carrier horses must be taken into consideration in any control program.

The site most often involved in the prolonged carriage of *S equi* is the guttural pouch. This site may become infected either during the early phase of infection or subsequent to internal rupture of retropharyngeal LNs. A resulting chronic empyema of this site may develop in up to 10% of affected animals. The purulent material may become inspissated and eventually form into discrete masses known as “chondroids”, which may be single or multiple and which can harbour *S equi*. The carrier state may persist in the guttural pouches for months to years. About half of horses with guttural pouch empyema cough sporadically and some may have an intermittent unilateral nasal discharge.

**Complications of *S. equi* infections**

The overall complication rate associated with *S equi* infection is approximately 20%1 and their occurrence may significantly increase case fatality rates.

**Metastatic spread**

*S equi* may potentially infect any anatomic site. The term bastard strangles is often used to describe metastatic spread with subsequent abscessation. Spread occurs primarily though hematogenous and lymphatic routes. Common secondary sites of infection include lung, mesenteric LNs, liver, spleen, kidneys, brain, sinuses and guttural pouches. Other rarer sites of infection have also been reported. It is important to note that there is no clinical or experimental evidence to suggest that antimicrobial therapy contributes to metastatic spread.

**Purpura haemorrhagica**

This is an aseptic necrotising vasculitis caused by the deposition of immune complexes in blood vessel walls. It results in widespread subcutaneous oedema, especially of the head and limbs, which in severe cases may result in oozing from skin surfaces and sloughing of the skin. Petechial and/or ecchymotic haemorrhages of the mucous membranes may also be observed. Risk factors associated with development of this complication are not known, but it is thought high pre-existing serum antibodies, especially IgA, to *S equi* may predispose to its development1.
Diagnosis

Culture

Culture of nasal swabs, nasal washes or pus aspirated from abscesses remains the “gold standard” for diagnosis of strangles. As *S. equi* are NOT part of the normal flora of the upper respiratory tract of horses, their isolation from these sites is considered significant. Samples should be plated on Columbia CNA agar with 5% sheep/horse blood added. The presence of other _-haemolytic Streptococci eg S. zooepidemicus may complicate interpretation, and specific biochemical tests (sugar fermentation) need to be conducted to differentiate these bacteria. Nasal washes are more effective than swabs for detection of small numbers of *S. equi* because a greater surface area within the internal nares is sampled. This involves instillation of ~50ml of warm normal saline via rubber tubing inserted to the level of the nasal canthus. The washings are then centrifuged and pellets cultured. False negative results may be obtained from culture if samples are collected during incubation and early clinical phases as *S. equi* is normally not present on the mucosa until 24-48 hours after the onset of fever.

Polymerase chain reaction (PCR)

Recently a PCR has been developed to the SeM of *S. equi* which provides a rapid and sensitive alternate for detection of *S. equi* in clinical samples. PCR is 3 times more sensitive than culture but does not distinguish between dead and live organisms and so a positive result must be considered presumptive until confirmed by culture. In addition, false negatives may occur in samples that contain polymerase inhibitors or abundant *S. equi*. PCR accompanying culture of a nasal swab or wash may be used in a control program to detect asymptomatic carriers, select animals for guttural pouch endoscopy, determine the success of elimination of *S. equi* from the guttural pouch of carriers after treatment, and to establish *S. equi* infection status prior to transportation and post transportation but prior to co-mingling.

Serology

Strong serum Ab responses are elicited to a wide range of surface exposed or secreted proteins of *S. equi* during infection or convalescence. Recently an ELISA specific for SeM has become commercially available in the USA. This ELISA has been used to detect recent infections, determine need for vaccination, identify animals with existing high concentrations of Ab that might predispose to purpura haemorrhagica, support a diagnosis of existing *S. equi* associated purpura haemorrhagica and support a diagnosis of bastard strangles. Although the SeM ELISA does not distinguish between vaccination and response to infection, comparison of sequential samples may assist interpretation.

Diagnosis of carriers

This is best achieved by direct visual assessment of both guttural pouches using endoscopy followed by cytological assessment, culture and PCR of lavage samples collected via the biopsy channel of the endoscope.

Treatment

Appropriate treatment of horses with strangles depends on the stages and severity of disease. It should be remembered that the majority of cases of strangles requires no treatment other than proper rest, a dry, warm stall and provision of soft, moist and palatable food of good quality while the disease runs its course.

Horses with early clinical signs

Immediate antibiotic therapy of horses with fever and signs of depression can be used in outbreaks of strangles. These horses may be identified by daily monitoring of rectal temperatures. Antibiotics may be given for 3-5 days and will prevent focal abscessation. However, treated horses are likely to remain susceptible to re-infection, especially if they continue to be exposed to infected horses during an outbreak.
Horses with LN abscessation that are alert

Once external lymphadenopathy is detected in an otherwise alert and health horse, antibiotic therapy is probably contra-indicated. At this stage antibiotics may help ameliorate the fever and lethargy, but also may prolong inevitable enlargement and rupture of the LN abscess. In these cases therapy should be directed towards enhancing maturation and drainage of abscess and may include topical application of hot packs, surgical drainage of matured LNs abscesses with daily flushing with 3-5% povidone iodine solution, and the use of nonsteroidal anti-inflammatory medications such as phenylbutazone in horses with normal hydration status.

Horses with LN abscessation that are anorexic and/or dyspnoeic

If horses are febrile, have signs of depression, anorexic and/or have dyspnoea as a result of upper airway obstruction then antibiotic therapy is indicated. Penicillin is considered the drug of choice, though cephalosporins and macrolides are possible alternatives depending on case of administration or site of infection. The use of trimethoprim-sulfadiazine (TMS) in strangles is controversial due to variable reports on in vivo efficacy. Antimicrobial therapy will usually be required for at least 2 weeks and in some cases up to 6-8 weeks depending on response to therapy. Intensive supportive therapy such as intravenous fluid therapy and tracheostomy may be needed in severe cases.

Horses with complications of infection

These horses should receive additional symptomatic therapy depending on the site and type of complication. For example, horses with metastatic abscesses frequently require long term antimicrobial therapy or drainage of abscesses if possible. Corticosteroids (at 0.1-0.2 mg/kg followed by a tapering dose regimen) are indicated in cases of purpura haemorrhagica together with appropriate antimicrobial therapy if active bacterial infections are suspected.

Treatment of Carriers

Therapy of guttural pouch empyema will depend on the consistency and volume of material within the pouches. Repeated lavage of pus-filled pouches via indwelling catheters using isotonic saline is recommended. In addition, administration of topical and systemic benzylpenicillin improves clearance. Topical therapy is recommended as a gelatin/penicillin combination to enhance deposition of the drug in this site. Use of a memory-helical polyprop retrieval basket may be required for non-surgical removal of large numbers of chondroids.

Control and prevention

Outbreak Investigation

Investigation of an outbreak of strangles should begin with collection of a comprehensive history and identification of affected groups of horses and their geographic location. A practical disease control strategy may then be implemented and could include cessation of all movement on and off the property and segregation of affected from non-affected horses through use of quarantine areas. Daily monitoring of rectal temperatures of exposed horses with prompt segregation and treatment of any newly febrile horses will help prevent spread as will bacteriological screening of exposed horses which can be moved to “clean” area if negative. Strict hygiene standards must be maintained during an outbreak and screening of convalescent cases should be conducted weekly via nasal washes to determine the status of shedding of S equi (PCR and/or culture) and endoscopy and lavage of guttural pouches for detection of carriers.

Hygiene Measures

Particular care should be taken to prevent indirect transfer of S equi from infectious horses (including potential subclinical carriers) to susceptible horses during an outbreak. Dedicated clothing and equipment should be used for infected horses, and non-infected horses should be handled before infected horses. Thorough cleaning (with particular care to remove any organic matter) and disinfection of equipment, stables, feed and water containers and horse transport in contact with infected horses is recommended, and manure and waste feed composted in an isolated location. Pastures used to hold
infectious animals should be rested for 4 weeks, but no evidence for prolonged survival of S equi on pastures exists.

**Vaccination**

Optimal immunity against S equi infection involves induction of both systemic and mucosal responses. Earlier whole cell (bacterin) vaccines have been largely superseded in North America, Australia and Europe by either vaccines containing extracts of S equi or attenuated live vaccines. The extract vaccines are given intramuscularly or subcutaneously together with an appropriate adjuvant. However, the efficacy of these extract vaccines is uncertain with little published data to support induction of significant protection. Occasional adverse reactions have been reported including soreness and abscesses at the injection site and occasional cases of purpura haemorrhagica. The live attenuated vaccines are comprised of a nonencapsulated strain of S equi with defects in carbohydrate utilisation. These may be administered intranasally (USA vaccines) or as an injection into horse's upper lip (UK vaccines), making sure an adequate amount of the vaccine reaches the pharyngeal and lingual tonsils. Safety issues include residual virulence with formation of slowly developing mandibular abscesses in a small % of vaccinates, swelling of the lip (vaccination site), nasal discharge and occasional cases of purpura haemorrhagica. In addition, as the vaccine contains live bacteria, accidental contamination of remote injection sites has resulted in abscess formation at these locations. Therefore, it is not recommended that other vaccines are administered concurrently with these vaccines.

Vaccine regimens for both vaccines involve 2-3 doses at 2 week intervals and then annual boosters. Pregnant mares may be boosted ~1 month prior to foaling. If horses are in high risk situations (e.g. kept in groups where new horses are regularly introduced, kept in premises where strangles has been diagnosed in the past) they may vaccinated at higher frequency e.g. every 3 to 6 months.

In outbreaks it is recommended that ONLY horses with NO known contact with infected horses or their exudates should be vaccinated with either vaccine type, and horses known to have had strangles within the previous year should not be vaccinated due to possible induction of purpura haemorrhagica. Use of the SeM ELISA may help in the prediction of possible adverse effects to vaccination.

**Quarantine and bacteriological screening**

Prevention of strangles through quarantine and screening of all horses introduced to a property is possible, but can be costly and time consuming. However, if possible all new horses should be isolated for 3 weeks and screened on 3 occasions, 1 week apart, by nasopharyngeal swabs or washes by culture and PCR. High standards of hygiene should be maintained between quarantined and resident horses. Further guidelines for prevention of strangles can be obtained from the Horserace Betting Levy Board in UK at http://www.hblb.org.uk.

**References**


