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Satellite Article

Sequelae and complications of *Streptococcus equi* subspecies *equi* infections in the horse

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Summary

***Streptococcus equi* ssp. *equi* infection in the horse, or strangles, commonly results in abscessation of the submandibular, submaxillary or retropharyngeal lymph nodes. Although this classical presentation of strangles is associated with a low mortality rate, complications and sequlae may worsen the prognosis and increase mortality rates. This article reviews sequelae and complictions of *S. equi* ssp. *equi* infection in the horse, including guttural pouch empyema, bastard strangles and immune mediated diseases such as purpura haemorrhagica, myopathies and myocarditis.**

Strangles, the disease caused by *Streptococcus equi* ssp. *equi* infection in the horse, is most frequently characterised by acute fever, upper respiratory catarrh and mucopurulent nasal discharge combined with acute submandibular and pharyngeal lymphadenopathy (Sweeney *et al.* 2005). The infectious agent responsible for the disease is a Gram-positive, β-haemolytic coccus frequently observed in chains. The bacterium is a specific pathogen of the horse. Transmission occurs via the oronasal route as organisms are shed in nasal secretions; however, fomites such as water troughs, tack, handlers and stall cleaning equipment may propagate bacterial spread from horse to horse (Sweeney *et al.* 1987a). The organism enters the oral or nasal cavity, attaches to the crypt cells of the lingual and palatine tonsils and invades deeper tissues. Within hours, organisms translocate into the mandibular and pharyngeal lymph nodes that drain this area (Sweeney *et al.* 2005). Virulence factors include a hyaluronic acid capsule and the *S. equi* M (SeM) protein, which inhibits phagocytosis and bactericidal mechanisms of neutrophils and macrophages (Sweeney *et al.* 2005).

Most commonly, *S. equi* infection results in abscessation of the submandibular, submaxillary and retropharyngeal lymph nodes; subsequent lymphadenopathy can result in upper airway obstruction and suffocation hence the name 'strangles'. Frequently, these abscesses rupture, drain and resolve with few to no additional complications or systemic illness. However, life threatening complications and costly sequelae can arise from *S. equi* infections in the horse. Rupture of retropharyngeal lymph node abscesses can result in guttural pouch empyema, chondroid formation and chronic carrier states (Knight *et al.* 1975; Ford and Lokai 1980; Sweeney *et al.* 1987b; Judy *et al.* 1999). Although the submaxillary, submandibular and retropharyngeal lymph nodes are the most common sites of abscessation, *S. equi* infection can potentially occur at any site in the body (Sweeney *et al.* 2005). The metastatic spread of *S. equi* and formation of abscesses in separate sites from the mandibular and pharyngeal region is more commonly known as 'bastard strangles' (Sweeney *et al.* 1987b). Common sites for metastatic strangles include the lung, mesentery, liver, spleen, kidneys and brain (Sweeney *et al.* 2005). In addition, other clinical manifestations of *S. equi* include immune mediated diseases such as purpura haemorrhagica, myopathies and myocarditis (Monlux 1961; Valberg *et al.* 1996; Pusterla *et al.* 2003; Sponseller *et al.* 2005; Sweeney *et al.* 2005; Kaese *et al.* 2005; Lewis *et al.* 2007). Complication such as bronchopneumonia, immune mediated responses and metastatic strangles dramatically increase mortality rates (Ford and Lokai 1980; Sweeney *et al.* 1987b,c; Sweeney 1996; Spoormakers *et al.* 2003). In strangles outbreaks, up to 20% of horses have been reported to develop complications or atypical manifestations of *S. equi*. Mortality rates during such outbreaks have been reported to range from 2.7–20% (Ford and Lokai 1980; Sweeney *et al.* 1987c; Spoormaker *et al.* 2003).

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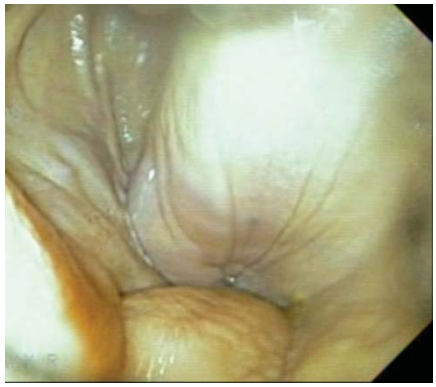

Fig 1: Retropharyngeal lymphadenopathy viewed along the floor of the medial compartment of the guttural pouch of a horse diagnosed with* S. equi. *Picture provided courtesy of the College of Veterinary Medicine, University of Georgia.

Classic *S. equi* infections most frequently occur in young horses ranging 1–5 years of age (Sweeney *et al.* 1987a). Clinical signs consisting of acute fever, depression and decreased appetite are first noted 2–6 days post exposure (Sweeney *et al.* 1987a). Lymphadenopathy is subsequently noted by Days 7–14; abscessed lymph nodes mature, rupture, drain and resolve with little to no additional complications. Typical strangles infections are characterised by high morbidity rates but low mortality rates.

Although mandibular and maxillary abscesses usually rupture and drain without further complications; retropharnyngeal lymph node abscessation can result in upper airway occlusion, which may be life threatening. Mature abscesses may subsequently rupture through the floor of the guttural pouch or into the pharynx resulting in guttural pouch empyema or bronchopneumonia, respectively (Sweeney *et al.* 1987b). Inspissated exudates in the guttural pouches often form chondroids (Ford and Lokai 1980; Judy *et al.* 1999; Sweeney *et al.* 2005).

Retropharyngeal lymphadenopathy is commonly diagnosed through endoscopic evaluation of the pharynx and guttural pouches; abscessed lymph nodes, empyema or chondroids may be visualised (**Fig 1**). Radiographs may depict a fluid line in the guttural pouches suggestive of empyema and tracheal compression from retropharyngeal lymphadenopathy. Chondroids within the guttural pouches can also be visualised radiographically (**Fig 2**).

Horses with chondroids or guttural pouch empyema may become asymptomatic carriers of *S. equi* bacteria, perpetuating recurrent herd outbreaks (Dalgleish *et al.* 1993; Newton *et al.* 2000; Sweeney *et al.* 2005). Although nasopharyngeal swabs may detect *S. equi* infection, culture and PCR testing of guttural pouch lavage samples are considered the gold standard for identification of asymptomatic carriers (Dalgleish *et al.* 1993; Newton *et al.* 2000). Guttural pouch lavage may be performed under endoscopic guidance with an open lumen catheter passed through the biopsy channel of the endoscope into the guttural pouch or by passage of a chamber's catheter into the guttural pouch (Sweeney *et al.* 2005). Horses with

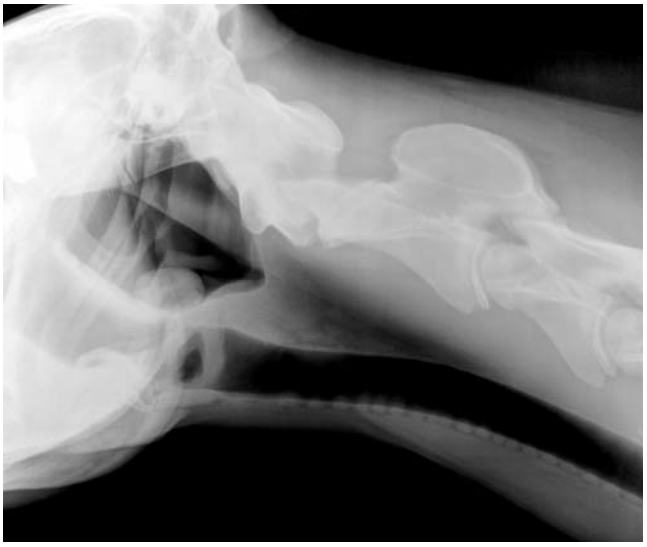

Fig 2: Note the chondroids depicted radiographically within the guttural pouch.

positive PCR tests or cultures should be quarantined and kept separate from negative, healthy horses.

Treatment of guttural pouch empyema requires repeated lavage of the guttural pouches with physiological solutions either transendoscopically, through an indwelling catheter or through a chambers catheter that has been passed into the pouches. A 20% acetylcysteine solution can be used to treat empyema; however, administration may be irritating to mucous membranes (Judy *et al.* 1999). Subsequently, penicillin gelatin solutions may be instilled into the guttural pouches to kill remaining bacteria (Judy *et al.* 1999; Sweeney *et al.* 2005). Chondroids may be removed by fragmentation and lavage or transendoscopically using forceps or a basket snare technique (Seahorn and Schumacher 1991). Larger chondroids may require surgical removal (Verheyen *et al.* 2000; Freeman and Hardy 2006).

After resolution of guttural pouch empyema or chondroids, horses should be retested for the presence of *S. equi* in the guttural pouches. Cultures or PCR tests on nasopharyngeal or guttural pouch lavages should be performed once a week for at least 3 weeks. Horses with 3 negative tests can be returned to the herd while positive horses should remain isolated and continue therapy (Sweeney *et al.* 2005).

Metastatic *S. equi* is characterised by lymph node abscessation in areas of the body separate from the mandibular or pharyngeal region. The bacteria may metastasise via haemotogenous spread, lymphatic routes or along connecting structures such as cranial nerves; as a result, abscesses may form anywhere in the body (Sweeney *et al.* 2005). Metastatic abscesses may occur subsequent to or in absence of submandibular or retropharyngeal lymph node abscesses. Common sites of metastatic abscesses include the kidneys, spleen, lungs, mesentery and brain (Ford and Lokai 1980; Raphel 1982; Spoormakers *et al.* 2003; Sweeney *et al.* 2005; Pusterla

et al. 2007). Specifically, reports of cervical, thoracic, paravertebral, prescapular, mesenteric and intra-abdominal lymph node abscesses along with gastrointestinal, myocardial, periorbital and cutaneous abscesses have been associated with *S. equi* (Ebert 1969; Rooney 1979; Ford and Lokai 1980; Sweeney *et al.* 1987c; Pusterla *et al.* 2007). In addition, metastasis of *S. equi* has been associated with septic arthritis, hepatitis, myocarditis, endocarditis, panopthalmitis, meningitis, meningioencephalomyelitis, pneumonia and periarticular cutaneous ulceration (Ebert 1969; Ford and Lokai 1980; Sweeney *et al.* 1987c; Dalgleish *et al.* 1993; Kaplan and Rush 1996; Meijer *et al.* 2000; Spoormakers *et al.* 2003; Finno *et al.* 2006).

Insidious clinical signs such as chronic weight loss, anorexia, lethargy and fever of unknown origin are characteristic of metastatic *S. equi*; however, depending on the organ system affected, clinical signs may be profound. Horses with intra-abdominal abscesses may present with signs of colic, fever, anorexia, depression and tachypnoea (Pusterla *et al.* 2007; **Fig 3**). Horses with neurological manifestations of *S. equi* may present with

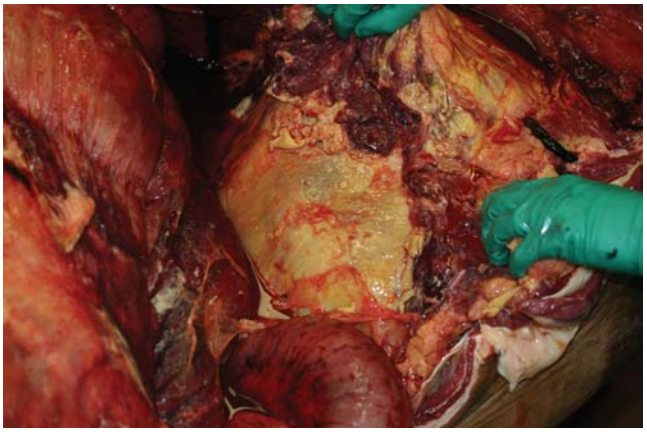

Fig 3: Metastatic* S. equi *with an intra-abdominal abscess and secondary diffuse peritonitis.

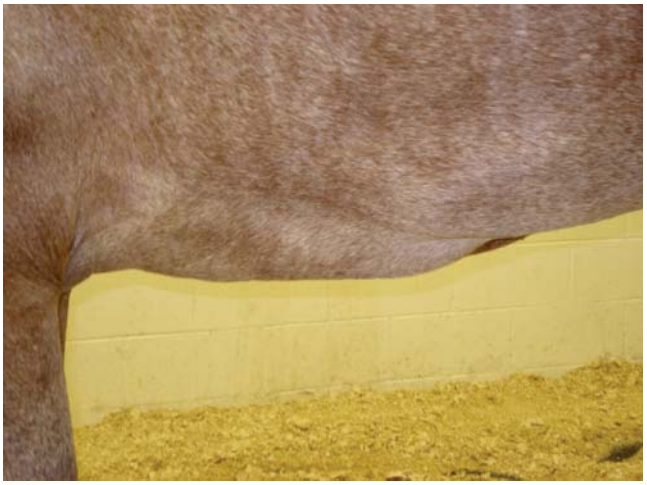

Fig 4: Ventral oedema in a horse diagnosed with purpura haemorrhagica secondary to* S. equi *infection.

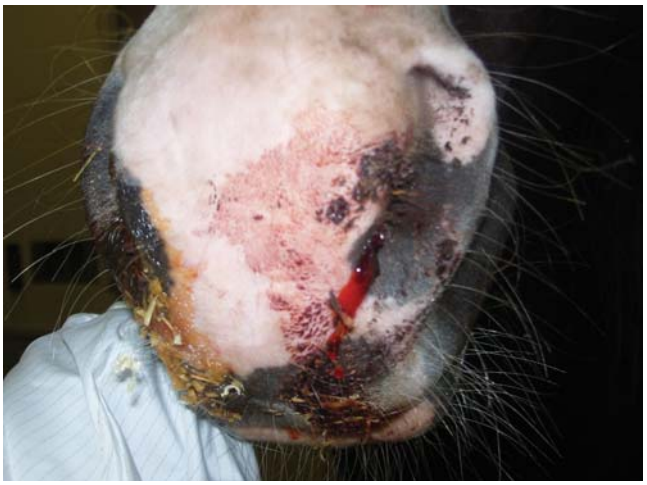

Fig 5: Unilateral epistaxis in a horse diagnosed with infarctive purpura haemorrhagica secondary to* S. equi *infection.

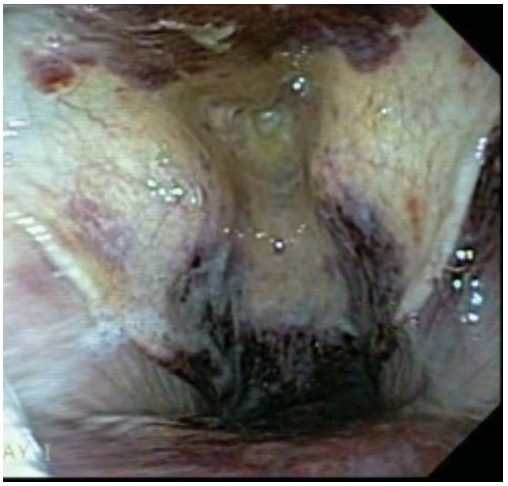

Fig 6: Ecchymosis along the pharyngeal wall viewed on upper airway endoscopy of a horse with purpura haemorrhagica secondary to* S. equi *infection.

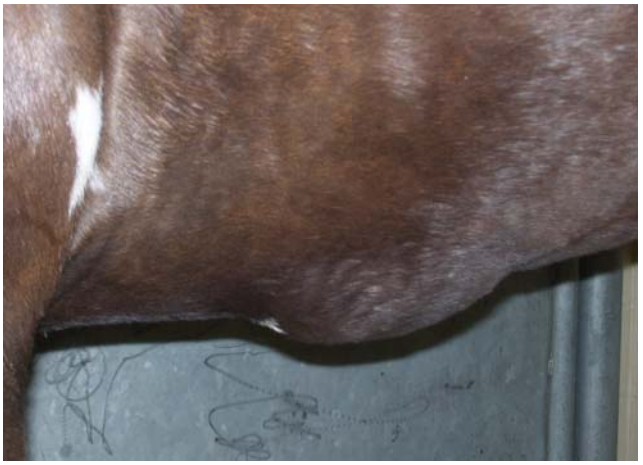

Fig 7: Muscle swelling located along the ventrum in a horse diagnosed with infarctive purpura haemorrhagica secondary to* S. equi *infection. Picture provided courtesy of the College of Veterinary Medicine, University of Georgia.

ataxia, hyperaesthesia, blindness, abnormal mentation, seizures, cranial nerve deficits and pain upon manipulation of the head and neck (DeLahunta 1977; Raphel 1982; Spoormakers *et al.* 2003; Finno *et al.* 2006). Arrhythmias and heart murmurs may be indicative myocardial abscesses or endocarditis resulting from metastatic *S. equi* (Ford and Lokai 1980; Kaplan and Rush 1996).

Bastard strangles may prove difficult to diagnose, particularly in cases with no history of the more typical clinical signs of strangles, such as submandibular or retropharyngeal lymph node abscessation. Clinical pathology consistently reveals mild anaemia, leucocytosis with mature neutrophilia, hyperfibrinogenaemia, hyperproteinaemia and hyperglobulinaemia (Pusterla *et al.* 2007; Whelchel *et al.* 2009). Rectal examination, abdominal ultrasonography (both percutaneous and transrectal), along with abdominocentesis are diagnostic methods of detecting abdominal abscesses. Peritoneal fluid may be cultured or submitted for PCR to detect the M protein gene. Thoracic radiographs and ultrasound may identify bronchopneumonia or pulmonary abscesses. Advanced imaging techniques such as magnetic resonance imaging (MRI) and computed tomography (CT) have proven beneficial in detecting brain abscesses (Spoormakers *et al.* 2003). Cerebral spinal fluid may be collected and submitted for the M protein PCR test (Finno *et al.* 2006).

Furthermore, marked elevation in the SeM specific ELISA (EBI)[1] titre is indicative of recent infection, recent vaccination, metastatic *S. equi* or purpura haemorrhagica (Sweeney *et al.* 2005). This test measures serum antibodies to the *S. equi* M protein and aids in the diagnosis of recent, but not necessarily current infections (Sweeney *et al.* 2005). Specifically, titres greater than or equal to 1:12,800 are strongly indicative of metastatic *S. equi*; however, titres between 1:3200 and 1:6400 have been found in confirmed cases of bastard strangles (Sweeney *et al.* 2005; Pusterla *et al.* 2007; Whelchel *et al.* 2008). Positive blood cultures for *S. equi* indicate septicaemia; however, negative blood cultures do not rule out metastatic *S. equi* (Kaplan and Rush 1996; Finno *et al.* 2006).

Treatment of metastatic *S. equi* consists of long-term antibiotic therapy with a Gram-positive or broad spectrum antimicrobial. Penicillin is considered the treatment of choice as *S. equi* is consistently susceptible to this antimicrobial. Based on a Gram-positive spectrum, cephalosporins, macrolides and trimethoprim-sulphadiazine (TMS) may also be used. Although frequently administered for broad spectrum antimicrobial coverage, *S. equi* resistance to aminoglycosides has been observed (Sweeney *et al.* 2005). The duration of antimicrobial therapy is often weeks to months. When possible, surgical drainage of abscesses should be performed. Although the prevalence rate of metastatic strangles is lower than classic strangles presentations, a 20% occurrence rate of complications or metastatic manifestations of *S. equi* has been reported in farm outbreaks (Ford and Lokai 1980; Sweeney *et al.* 1987c). Metastatic infections are associated with a poor prognosis, especially in cases of central nervous system, respiratory, cardiovascular or gastrointestinal involvement (Ford and Lokai 1980). However, Pusterla *et al.* (2007) reported a 40% survival rate in patients diagnosed with abdominal abscesses due to *S. equi*. Advanced diagnostics may lead to earlier detection and treatment of these abscesses, increasing survival rates.

Due to the risk of purpura haemorrhagica, horses with concurrent bastard strangles should not be vaccinated with either the killed i.m. or the attenuated live intranasal vaccine. Post recovery, SeM ELISA titres should be checked prior to vaccination. Horses with SeM titres greater than 1:1600 should not be vaccinated at that time and horses with titres greater than 1:3200 should never be vaccinated for strangles (Sweeney *et al.* 2005).

Other clinical manifestations of *S. equi* include immune mediated processes such as purpura haemorrhagica, myopathies and myocarditis (Sweeney *et al.* 2005). Purpura haemorrhagica is an immune mediated vasculitis and *type 3* hypersensitivity response characterised by antibody-antigen complex deposition in blood vessel walls. Immune complexes stimulate complement activation and chemoattractants, resulting in neutrophil and macrophage infiltration. Inflammatory cells release proteolytic enzyme resulting in vessel wall damage and subsequent oedema (Morris 2002). Vasculitis may affect the integument, gastrointestinal tract, lungs, muscle and laminae resulting in complications including laminitis, colic, respiratory distress and muscle pain (Sweeney *et al.* 2005).

Purpura haemorrhagica may present as a sequela to *S. equi* infection, occurring 2–3 weeks post infection or subsequent to administration of strangles vaccines. Horses with previously high antibody titres to *S. equi* may be predisposed to developing purpura post vaccination or natural exposure (Sweeney *et al.* 2005). In cases of purpura haemorrhagica following *S. equi* infection, bacterial antigens and IgA antibody complexes can be detected in the serum of these horses (Galan and Timoney 1985). Although *S. equi* is a common cause of purpura haemorrhagica, other viral and bacterial infections may trigger this hypersensitivity reaction.

Clinical signs of purpura haemorrhagica consist of pyrexia along with pitting oedema in the distal limbs, ventrum, prepuce, pectoral region and head; in severe cases, sloughing of the skin of the distal limbs may occur (**Fig 4**). Petechial and ecchymotic haemorrhages are often visible on mucous membranes, and mild epistaxis can occur (**Fig 5**). Urticaria may also be observed. Further signs of colic, diarrhoea, laminitis and respiratory distress may result from systemic vasculitis (Sweeney *et al.* 1987b, 2005; Morris 2002; Pusterla *et al.* 2003).

Purpura haemorrhagica in horses is similar in both clinical signs and pathophysiology to Henoch Schönlein purpura (HSP) in man. HSP is a systemic small vessel, immune mediated vasculitis characterised by purpuric

lesions, abdominal pain, gastrointestinal haemorrhage, arthritis, soft tissue oedema, and occasionally renal disease (Meiller *et al.* 2008; Yang *et al.* 2008). The syndrome is more commonly seen in children compared to adults. A variety of infectious agents, including beta-haemolytic *streptococcus*, are thought to trigger HSP. Skin biopsies of affected areas may reveal a leucocytoclastic vasculitis with IgA and C3 deposition whereas renal biopsies show signs of mesangial nephropathy characterised by IgA deposition (Meiller *et al.* 2008). Human cases of HSP have been successfully treated with high doses corticosteroids and immunosuppressive agents such as cyclophosphamide and azathioprine (Meiller *et al.* 2008).

A diagnosis of purpura haemorrhagica is often based on clinical signs and response to therapy; however, a definitive diagnosis requires a full thickness punch biopsy of the skin demonstrating a leucocytoclastic vasculitis (Morris 2002; Sweeney *et al.* 2005). Complete blood cell count typically reveals leucocytosis, mature neutrophilia and mild anaemia. Serum chemistry often shows hypoalbuminaemia, hyperglobulinaemia and hyperfibrinogenaemia (Morris 2002; Pusterla *et al.* 2003). Upper airway endoscopy may aid in visualisation of petechia and ecchymosis present in the nasopharyngeal regions (**Fig 6**). Marked elevations in SeM titres (≥1:12,800) for *S. equi* are commonly detected in cases of purpura haemorrhagica (Sweeney *et al.* 2005).

Therapy for purpura haemorrhagica consists mainly of immunosuppressive therapy and supportive care. Corticosteroids such as dexamethasone (0.04–0.2 mg/kg bwt once a day given i.v., i.m. or *per os* in the morning) and prednisolone (0.5–1.0 mg/kg bwt once a day *per os*) can be administered until remission of clinical signs is achieved. Subsequently, dosages should be gradually tapered over a course of 2–4 weeks; premature cessation of steroid therapy may result in a clinical relapse (Pusterla *et al.* 2003). Antimicrobial therapy can be instituted to reduce the antigenic load in horses with an existing focus of infection and to prevent secondary infections. In cases of *S. equi* infection, systemic penicillin therapy should be initiated (22,000 u/kg bwt procaine penicillin G i.m. every 12 h or potassium penicillin i.v. every 6 h). Nonsteroidal anti-inflammatory therapy may also be instituted. Hydrotherapy and pressure bandaging of the lower limbs should be implemented to minimise oedema of the limbs (Morris 2002; Pusterla *et al.* 2003).

Infarctive purpura haemorrhagica is a rare and usually fatal manifestation of purpura haemorrhagica characterised by infarctions occurring in muscle, lung and the gastrointestinal tract subsequent to the immune mediated vasculitis triggered by *S. equi* infections. Systemic vasculitis leads to infarction and haemorrhage in various tissues as well as to early stages of disseminated intravascular coagulopathy (Valberg *et al.* 1996; Kaese *et al.* 2005; Valberg 2006). Horses with muscle infarctions appear stiff, reluctance to move, and have well-demarcated swellings in various muscle groups (**Fig 7**). Infarctions occurring in other tissues can lead to signs of colic and respiratory distress. The more common signs of petechia, ecchymosis and oedema observed with purpura haemorrhagica are also apparent.

Diagnostically, a complete blood count reveals signs of acute inflammation (neutrophilia, elevated immature neutrophils) while blood chemistry shows hyperproteinaemia with concurrent hypoalbuminaemia along with marked elevations in creatinine kinase (CK) and aspartate aminotransferase (AST) (Valberg *et al.* 1996; Sweeney *et al.* 2005; Kaese *et al.* 2005; Valberg 2006). Myoglobinaemia and myoglobinuria may be evident. A coagulation panel may show prolonged clotting times and increased D-dimers (Kaese *et al.* 2005). These patients typically have very high SeM titres (≥1:12,800); however, a definitive diagnosis is based on histopathological evidence of a leucocytoclastic vasculitis and acute coagulative necrosis in affected muscle tissues (Valberg 2006).

Treatment consists of aggressive immunosuppression with corticosteroids (dexamethasone 0.1 mg/kg bwt i.v. every 24 h), potassium penicillin therapy (22,000–44,000 u/kg bwt i.v. every 6 h), 10% dimethyl sulphoxide (DMSO, 100 mg–1 g/kg bwt i.v. as a 10% solution every 24 h), vitamin E (6000 u *per os* q. 24 h), i.v. fluids, and analgesics (lidocaine, butorphanol or ketamine at a constant rate of infusion) (Kaese *et al.* 2005). Plasma may be administered to replenish clotting factors and anti-thrombin, while other anti-coagulative therapies such as low molecular weight heparin, unfractionated heparin and aspirin may be instituted.

In addition, 2 other myopathies associated with *S. equi* infection have been described primarily in Quarter Horses: an acute rhabdomyolysis and immune mediated polymyositis. The acute rhabdomyolysis is a rare and usually fatal sequela to *S. equi* infection. Currently, the only reported cases have been described in Quarter Horses younger than 7 years of age (Valberg *et al.* 1996; Sponseller *et al.* 2005). Clinically, the acute rhabdomyolysis and infarctive purpura haemorrhagica syndromes are similar; however, the 2 disorders are thought to have distinct pathophysiologies. Horses with acute rhabdomyolysis secondary to *S. equi* infection demonstrate a stiff gait accompanied by acute, painful, firm muscle swellings in the epaxial and gluteal muscles; these clinical signs are often seen concurrently with submandibular lymphadenopathy or guttural pouch empyema (Sponseller *et al.* 2005; Valberg 2006). Clinical pathology reveals an inflammatory leucogram (neutrophilia and hyperfibrinogenaemia) along with marked elevations in CK and AST. Myoglobinaemia and myoglobinuria may result from the severe degree of rhabdomyolysis. In a report of 4 horses with acute rhadomyolysis subsequent to *S. equi* infection, SeM titres were normal while Se18.9 titres were elevated in 3 horses (Sponseller *et al.* 2005). Se18.9 is a fibrinogen binding protein that has recently been described as an antiphagocytic virulence factor for *S. equi*

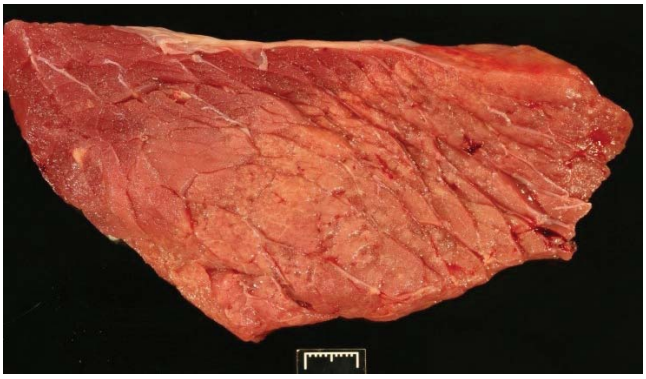

Fig 8: Muscle cross section from a horse diagnosed with acute rhabdomyolysis secondary to* S. equi *infection. Note the pale colour of the abnormal muscle compared areas of more normal muscle in the cross section.

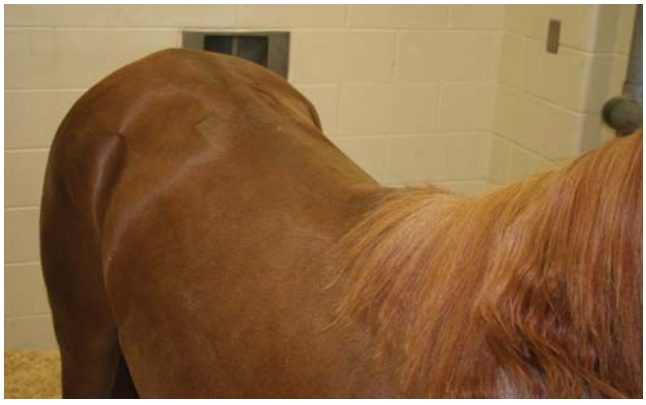

Fig 9: Gluteal and epaxial muscle atrophy in a horse diagnosed with immune mediated myositis secondary to* S. equi *infection. Diagnosis of immune mediated myositis was verified on epaxial muscle biopsy.

(Tiwari *et al.* 2007). Histopathology of affected skeletal muscles reveals a severe acute muscle necrosis with macrophage infiltrates (Valberg 2006; **Fig 8**). Although the pathogenesis remains unclear, a superantigen immune response (similar to human toxic shock-like syndrome) or muscle damage from local release of exotoxins have been implicated. Furthermore, any potential role of the Se18.9 virulence factor remains unknown (Sponseller *et al.* 2005; Valberg 2006).

Reported therapy consists of dexamethasone, i.v. penicillin, DMSO, flunixin meglumine, vitamin B12, vitamin E and selenium. Lidocaine, detomidine or ketamine may be administered at a constant rate of infusion for analgesia (Sponseller *et al.* 2005). Despite aggressive efforts, pain progresses and patients may become recumbent, necessitating humane euthanasia (Sponseller *et al.* 2005; Valberg 2006).

The final myopathy associated with *S. equi* infection in the horse is an immune mediated polymyositis (IMM) characterised by general malaise, stiffness and acute atrophy of the epaxial and gluteal muscles (**Fig 10**). The syndrome is predominantly described in Quarter Horses, and frequently, these horses have a history of recent exposure to *S. equi* (ssp. *equi* or *zooepidemicus*), or other respiratory disease (Valberg *et al.* 1996; Valberg 2006; Lewis *et al.* 2007). Serum CK and AST levels are frequently elevated. Histopathology of affected muscle tissues reveals a hallmark lymphocytic infiltrate in muscles fibres along with fibre necrosis, macrophage infiltration, and fibre regeneration (Valberg *et al.* 1996; Valberg 2006; Lewis *et al.* 2007). In the report by Lewis *et al.* (2007), immunohistochemical analysis of 7 muscle biopsies from cases of equine IMM identified an increased ratio of CD4+ to CD8+ lymphocytes and muscle tissues did not show specific staining for equine IgG (Valberg 2006; Lewis *et al.* 2007). These findings suggest equine IMM may be due to a cell mediated response vs. a humeral response. However, Valberg *et al.* (1996) reported of a progressive muscle atrophy secondary to rhabdomyolysis where immunohistochemistry of muscle biopsies stained positive for IgG.

In addition to the immune mediated myopathies triggered by *S. equi*, bacterial antigens may trigger an immune mediated myocarditis. In reported cases, a nonsuppurative myocarditis was described alongside concurrent pharyngeal lymphadenopathy. *S. equi* ssp. *equi* and ssp. *zooepidemicus* were isolated from abscessed lymph nodes. Biopsies of cardiac muscle revealed a lymphocytic and macrophage infiltrate in the myocardium; however, bacteria were not observed. The myocarditis documented in these patients was suspected to result from an immune-mediated response triggered by *Streptococcus* antigens or from bacterial toxins causing tissue damage (Monlux 1961; Sweeney *et al.* 2005).

In conclusion, guttural pouch empyema, bastard strangles and immune mediated diseases are potential sequelae to *S. equi* infections in the horse. Although the classical presentation of strangles is associated with a low mortality rate, the complications and sequelae described above are associated with both increased mortality rates and a more guarded prognosis. Prompt recognition of atypical manifestations and sequelae to *S. equi* is necessary to identify, treat, and improve the prognostic outcome for these patients. Furthermore, recognising uncommon presentations and clinically silent carriers is necessary to prevent dissemination of *S. equi* to other horses.

Manufacturer's address

[1]IDEXX, Lexington, Kentucky, USA.

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