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Review Article

Strangles and its complications

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Summary

Strangles, caused by the Gram-positive bacteria *Streptococcus equi* subspecies *equi* (*S. equi*), is a highly contagious upper respiratory infection in horses. The infection is transmitted by inhalation or direct contact with mucopurulent discharge from an infected animal, resulting in fever, depression, and submandibular and retropharyngeal lymph node enlargement that can lead to respiratory distress. Complications include secondary cellulitis at external abscessation sites, guttural pouch empyema and its persistence into the carrier state, purpura haemorrhagica, metastatic abscessation, emergency tracheostomies and rarely secondary *S. equi* pneumonia or myositis. Control of outbreaks requires strict isolation protocols and hygiene measures. Detection methods of the index case and carrier state are constantly being refined to assist in the identification and prevention of disease perpetuation.

Introduction

Strangles is a worldwide, contagious acute upper respiratory infection in horses, resulting in high morbidity but low mortality (Sweeney *et al.* 1989, 2005; Duffee *et al.* 2015). It is a reportable disease in many countries and some states in the United States. Strangles is caused by the Gram-positive cocci *Streptococcus equi* subspecies *equi* (*S. equi*). The infection is characterised by fever, lethargy, purulent nasal discharge and regional lymph node abscessation. Highly concentrated and transient populations are at greater risk of contracting the disease (Sweeney *et al.* 1989, 2005).

Pathophysiology

Streptococcus equi is inhaled or ingested after direct contact with mucopurulent discharge from infected horses or contaminated equipment. The bacterium attaches to the crypts and epithelium of the lingual and palatine tonsils with the assistance of the fibronectin binding surface proteins, *SeM* and *SEQ2190*. The organism does not colonise the mucosal surface but penetrates into deeper tissue and enters the mandibular and pharyngeal lymph nodes. The hyaluronic acid capsule and surface proteins allow the bacterium to avoid phagocytosis by neutrophils. Clinical signs develop 3–14 days after exposure (Lannergard *et al.* 2005; Sweeney *et al.* 2005; Robinson *et al.* 2013).

Clinical signs

The severity of clinical signs of strangles can vary depending on the previous exposure of the individual horse. The first clinical sign of classical strangles disease is usually acute onset fever (often >103°F [39.4°C]) which may be missed by caretakers if the horse continues to eat. It is then followed by lethargy, depression, bilateral mucopurulent discharge, lymphadenopathy and abscessation most commonly of the retropharyngeal and mandibular lymph nodes (**Figs 1** and **2**). Early cases may only show sensitivity on palpation of the retropharyngeal area without obvious swelling. Occasionally, the parotid and cranial cervical lymph nodes are affected and have been misidentified as foreign bodies or trauma. *Streptococcus equi* abscessation can occur at the site of any subcutaneous lymph node and have been seen in unusual locations such as ventral to the eye with *S. equi* positive purulent drainage from the medial canthus (**Fig 3**). Secondary cellulitis of the surrounding tissues can develop after drainage occurs if proper hygiene is not maintained. Clinical signs are more severe in immunologically naive (1–5 years of age), geriatric (older than 20 years) and immunocompromised horses, whereas mature horses with some immunity often have a milder version of the disease called 'atypical' or 'catarrhal' strangles. These horses can present with only nasal discharge and small abscesses (if any) and rapid resolution of disease. Strangles is often overlooked as a differential by veterinarians and owners in these cases, representing a significant biosecurity risk for they shed virulent *S. equi* that can produce significant disease in the naïve population (Sweeney *et al.* 1989, 2005).

Transmission and immunity

Shedding of *S. equi* begins 2–3 days after onset of fever providing a window during which febrile horses can be segregated, but also a period of false negatives when performing diagnostic tests. In most cases, shedding persists for a minimum of 2–3 weeks but often as long as 6 weeks (Sweeney *et al.* 2005). If organisms are harboured in the guttural pouches, horses can shed *S. equi* for months or years. These outwardly healthy horses (*S. equi* carriers) that still shed organisms are the source of infection when introduced into a new population of horses (Newton *et al.* 1997a,b, 2000; Verheyen *et al.* 2000). Transmission occurs through nose-to-nose contact and fomites. Organism could be cultured off surfaces in an environmental field setting experiment for only 3 days (Weese *et al.* 2009), but moist environments (e.g. water buckets) are known to allow the organism to persist for extended periods (Sweeney *et al.* 2005).

A total of 75% of horses that have been infected with *S. equi* and have not been treated with antimicrobials develop waning immunity for approximately 5 years (Todd 1910). Foals of mares that have recovered from strangles are usually protected by maternal antibodies until weaning (Hamlen *et al.* 1994; Sweeney *et al.* 2005).

Fig 1: Nasal discharge in a horse with strangles.

Fig 2: Enlarged submandibular lymph node in a foal with strangles. Image courtesy Dr S. Berkowitz, Unionville, Pennsylvania, USA.

Complications

Guttural pouch disease and persistent carriers

Retropharyngeal lymph node enlargement can result in narrowing of the pharynx, whether or not external swelling of the retropharyngeal area is visible. This results in respiratory stridor/stertor, dysphagia and neck extension. Horses may develop respiratory distress requiring emergency tracheotomy. Upper airway endoscopy often reveals a narrowed pharynx due to axial deviation of the guttural pouches and enlarged retropharyngeal lymph nodes are visible, bulging through the respiratory mucosa on the floor of the guttural pouch. Empyema results when the

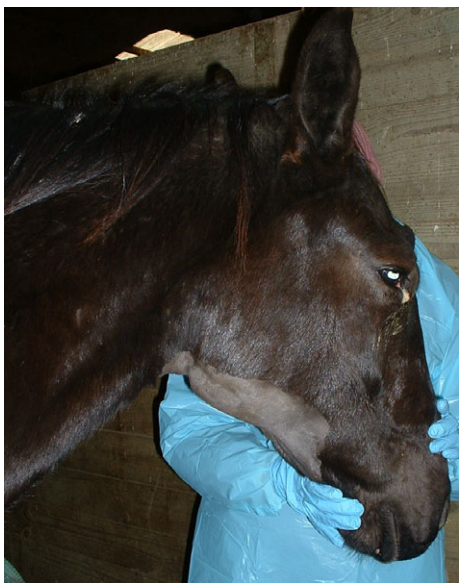

Fig 3: Streptococcus equi positive purulent ocular discharge. Image courtesy Dr E. Koch, Wolfeboro, New Hampshire, USA.

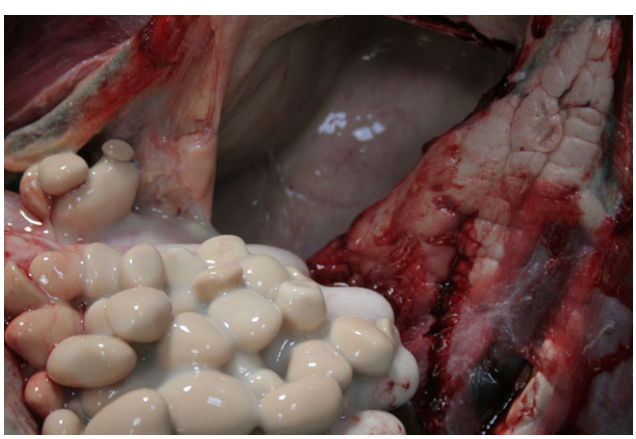

Fig 4: Chondroids in an open guttural pouch at necropsy. Image courtesy Dr J. Engiles, Kennett Square, Pennsylvania, USA.

retropharyngeal lymph nodes drain into the guttural pouches on the floor of the medial compartment. On endoscopic examination, drainage from the opening of the guttural pouch with difficult entry is highly suggestive of guttural pouch empyema, but certainly not a requirement for the presence of *S. equi*. Dysphagia is the most common neurological sign in horses with strangles and may be secondary to pharyngeal pain, swelling, or cranial nerve inflammation secondary to guttural pouch disease. Aspiration pneumonia due to *S. equi* has been seen in horses with severe dysphagia secondary to strangles. Horses with guttural pouch empyema can develop into persistent asymptomatic carriers of *S. equi*. Inspissated pus (chondroids) can develop in the guttural pouch (**Fig 4**) while the horse has a normal outward appearance. The guttural pouch can be grossly normal and still carry *S. equi* in a microscopic biofilm and therefore microbiological conformation of the absence of *S. equi* is required to rule out the horse being a carrier. Prevalence of carrier status after an outbreak can be as high

as 40% and has been documented for up to at least 2 years (Newton *et al.* 1997b; Duffee *et al.* 2015).

Bastard strangles (metastatic abscessation)

Previous reports show that in as low as 2% (Duffee *et al.* 2015) to as high as 20% (Sweeney *et al.* 2005) of cases, *S. equi* spreads via the haematic or lymphatic systems from an existing abscess. This results in metastatic abscessation (also known as bastard strangles) and can affect any organ system. Clinical signs depend on the organ system involved. As previously mentioned, aspiration of mucopurulent discharge or haematogenous or lymphatic spread to the lungs can cause pneumonia. Metastatic abscessation can occur and the most common sites are the mesentery, liver, spleen and kidneys, leading to peritonitis and clinical signs of colic (**Fig 5**). Abscessation of the cranial mediastinal lymph nodes can cause tracheal compression and respiratory distress. Myocarditis (Ford and Lokai 1980), endocarditis, panophthalmitis (Kaplan and Moore 1996), mastitis (Bergsten and Persson 1966), tenosynovitis (Rossdale and Ricketts 1974), arthritis (Dalgleish *et al.* 1993; Meijer *et al.* 2001) and paravertebral abscesses (Rooney 1979) are rare but have been reported. Neurological signs are present when abscessation occurs in the brain. Computed tomography and magnetic resonance imaging have successfully imaged abscesses within the cerebral cortex (Allen *et al.* 1987; Cornelisse *et al.* 2001; Spoormakers *et al.* 2003). The presence of bastard strangles can increase the mortality rate to as high as 62% (Ford and Lokai 1980).

Purpura haemorrhagica

Purpura haemorrhagica is an aseptic necrotising vasculitis that can occur in mature horses after repeated natural exposure to infection or after vaccination of horses that have had strangles. Although commonly associated with *S. equi*, pupura haemorrhagica can occur in response to a number of different pathogens, such as *Streptococcus zooepidemicus*, *Rhodococcus equi* and *Corynebacterium pseudotuberculosis* (Morris 1987; Pusterla *et al.* 2007). The actual incidence of this *type 3* hypersensitivity response secondary to strangles or vaccination is unknown (Galan and Timoney 1985; Sweeney *et al.* 2005). A report from 1999 noted 2 cases of purpura-like disease per 100,000 doses of live attenuated intranasal *S. equi* ssp. *equi* vaccine sold (Timoney 1999). Pusterla *et al.* (2003) noted that 5 out of 53 cases of purpura haemorrhagica had a history of *S. equi* killed extract intramuscular (i.m.) vaccination and 17 had a history of *S. equi* disease or exposure. Clinical signs range from mild to life-threatening, including pitting oedema of the head, trunk and distal limbs as well as petechiation and ecchymoses of the mucous membranes. In some cases, antigen-antibody complexes affect other sites, including the gastrointestinal tract, muscles, lungs and kidneys. Diagnosis can be confirmed with a skin biopsy consistent with a leucocytoclastic vasculitis.

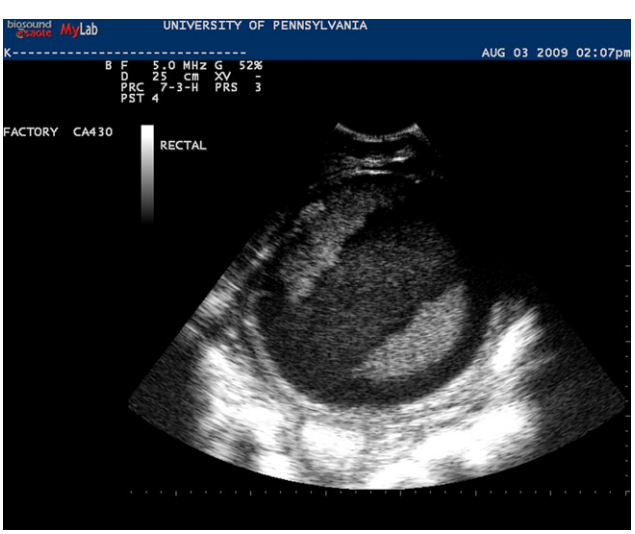

Fig 5: Ultrasound image of an intra-abdominal abscess in a horse with metastatic* S. equi *infection. Image courtesy Dr D. Short, Pullman, Washington, USA.

Myositis

Muscle infarctions and rhabdomyolysis with progressive atrophy are 2 separate myopathies that can occur secondary to *S. equi* exposure. *Streptococcus equi* myopathies can occur as part of a purpura haemorrhagica episode but can also occur solely secondarily to exposure to or concurrent infection with *S. equi.* Both are thought to be immune-mediated in origin and will have creatinine kinase values ranging from 200,000 to 1,000,000 u/l. Muscle infarctions are secondary to an immune-mediated vasculitis associated with purpura haemorrhagica. Many of these horses have severe myonecrosis and are often acutely recumbent with associated infarctions of muscle, skin, lungs and gastrointestinal tract and *SeM* titres may exceed 6400. These horses often have a poor prognosis despite intravenous (i.v.) penicillin therapy (85% mortality) and corticosteriodal therapy if not recognised early. Less severely affected horses with a recent history or exposure of *S. equi* may recover from acute recumbency and experience significant muscle mass loss associated with a lymphocytic immune-mediated polymyositis. It is most commonly seen in Quarter Horse related breeds. This rhabdomyolysis with progressive atrophy is thought to be caused by an immune-mediated reaction due to cross-reactivity between *SeM* and myosin. Treatment with corticosteroids and antibiotics will often return muscle mass to normal (**Fig 6**) (Valberg *et al.* 1996; Sponseller *et al.* 2005; Sweeney *et al.* 2005; Valberg 2015).

Diagnostics

Early definitive diagnosis is essential for containing this highly infectious disease but can be difficult with diagnostic testing sensitivities as low as 40% in the early stages of disease due to low levels of bacteria, absence of disease shedding (Lindahl *et al.* 2013) and *S. equi* fragility once outside the horse. Pristine sample handling and quick efficient transportation of *S. equi* to the laboratory is vital. In addition, the presence of organic debris in clinical samples can inhibit polymerase chain reaction (PCR), hence false negatives can occur. Complete blood counts are often characterised by leucocytosis with a mature neutrophilia, anaemia and hyperfibrinogenaemia and can provide suggestion for *S. equi* testing in an index febrile horse (Ijaz *et al.* 2010, 2011; Duffee *et al.* 2015). Obvious, mature external abscesses can be aspirated for cytological evaluation that will reveal Gram-

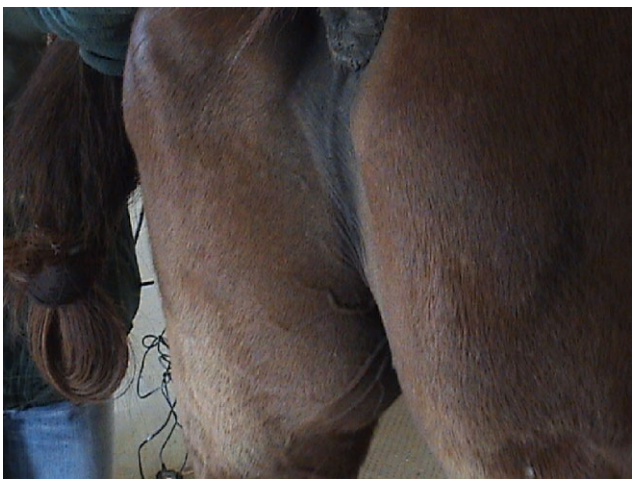

Fig 6: Bilateral semimembranosus and semitendinosus muscle atrophy secondary to S. equi associated immune-mediated polymyositis.

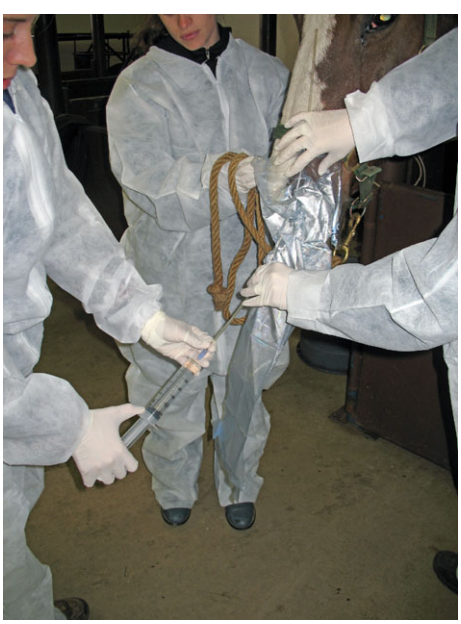

Fig 7: Nasopharyngeal wash sampling performed for S. equi diagnostics. Briefly, the horse is sedated and a uterine pipette punctured from the outside to the inside of a rectal sleeve. The rectal sleeve is placed over the horse's nose and the pipette passed up the ventral meatus to the level of the pharynx at which time 50 ml sterile saline is infused. The rectal sleeve then catches the nasopharyngeal lavage sample via gravity flow.

positive extracellular cocci in long chains to confirm a beta-haemolytic infection, but not confirm *S. equi*. Diagnosis via culture or PCR can be obtained from aspirates of mature abscesses, nasopharyngeal washes (**Fig 7**), or guttural pouch washes (Sweeney *et al.* 2005; Holland *et al.* 2006). Swabs of the rostral nasal passage have poor sensitivity unless the animal has obvious nasal discharge (Lindahl *et al.* 2013). Nasopharyngeal swabs (via an unguarded uterine culture swab) have been commonly used, but nasopharyngeal washes have been found to be more sensitive presumably due to the larger surface area of respiratory epithelium sampled (Lindahl *et al.* 2013; Boyle *et al.* 2015). Historically, *S. equi* bacterial culture was considered the gold standard for diagnosis, but has been shown repeatedly to have poor sensitivity when dealing with low levels of infection (early disease stages or carriers). Polymerase chain reaction for the detection of DNA has been shown to be more sensitive, although more expensive, while supplying same day or next day results (Boyle *et al.* 2012a,b, 2015, 2016; Lindahl *et al.* 2013; Webb *et al.* 2013). Detection of early cases of strangles can be improved by multiple samples taken from the same horse on the same day (Lindahl *et al.* 2013). The triplex PCR (Webb *et al.* 2013) is considered the gold standard for PCR strangles diagnosis due to its increased sensitivity and specificity by looking for 3 different superantigens on the *SeM* gene. This is currently not available in the United States, but the *SeeI* PCR (Baverud *et al.* 2007) is still much more sensitive than the culture (Boyle *et al.* 2012a,b, 2015, 2016 Lindahl *et al.* 2013). The combination of PCR and culture will further increase the sensitivity of *S. equi* recovery and this combination should be the diagnostic test of choice for nasopharyngeal washes and guttural pouch lavages. Many laboratories already offer this combination for the same price as the PCR alone, but may not advertise that they are providing both services. Polymerase chain reaction negative but culture positive samples (PCR false negatives) are possible (Grønbaek *et al.* 2006). It is argued that PCR false positives occur due to the detection of 'dead DNA', although others argue that dead *S. equi* bacteria cannot adhere to the respiratory mucosal surfaces and would not be present in the horse. The mucociliary clearance in the nasopharynx is highly efficient at removing particles including DNA. In addition, clinical evidence of disease transmission has occurred from horses with PCR positive, culture negative guttural pouch washes to a naïve population, supporting that this bacteria was alive and infectious, just below of the limit of detection for the *S. equi* bacterial culture (Waller 2014).

Carriers can appear outwardly healthy but harbour *S. equi* in their guttural pouches. Definitive determination of carrier status requires endoscopic examination of the guttural pouches as well as the combination of PCR testing and culture of guttural pouch fluid (Newton *et al.* 1997a,b; Verheyen *et al.* 2000; Sweeney *et al.* 2005; Waller 2014; Boyle *et al.* 2015, 2016). Cases of metastatic abscessation may be characterised by anaemia of chronic disease. Rectal examination, abdominal ultrasonography and rectal ultrasonography of cases suspected of having metastatic abscessation often reveal an intra-abdominal mass. Chemistry profiles reflect abnormalities indicative of the body system affected in bastard strangles and purpura haemorrhagica. The latter disease often produces an abnormal coagulation profile (Sweeney *et al.* 2005; Pusterla *et al.* 2007).

Two types of serological tests are currently available. One involves the use of an ELISA to detect the surface protein *SeM* and is available in the United States. This test has been useful for detecting recent (4–6 weeks), but not current infection; identifying horses that may be predisposed to, or diagnosed with, purpura haemorrhagica and diagnosing *S. equi* metastatic abscessation (titres often ≥12,800) (Sweeney *et al.* 2005). It has been shown that the *SeM* ELISA is not associated with the identification of carrier horses (Davidson *et al.* 2008). A more recently developed serological test available in the UK evaluates for 2 surface proteins; *SEQ2190* and *SeM*. This test detects animals that

have seroconverted within 2 weeks of infection and can be a preliminary screening for persistently infected animals (Robinson *et al.* 2013). Seropositive horses can be identified prior to arrival on a new farm or during quarantine. Guttural pouch endoscopy and PCR and culture combination on the lavage is then performed to identify *S. equi* carriers. Unfortunately, if the horse was previously vaccinated, the source of the antibody response measured on these serological tests cannot be determined (Waller 2014).

Treatment

The goal of treating strangles is to control transmission and eliminate infection while providing future immunity to the disease. Uncomplicated cases of strangles are often left to run their course with supportive care, providing immunity that wanes over time. Isolation in a clean, dry stall and moist, palatable food should be available. Nonsteriodal anti-inflammatories should be used judiciously to decrease swelling and promote eating. Hot compresses or topical 20% ichthammol can be used to accelerate maturation of abscessation. Mature external abscesses should be lanced to allow drainage, followed by daily lavage of open abscesses using 3–5% povidone iodine solution. This expedites resolution of abscessation as well as alleviation of compression of surrounding structures, such as the pharynx.

The use of antimicrobials for treating strangles is controversial. The preferred antimicrobial is penicillin (procaine penicillin [22,000 to 44,000 iu/kg bwt i.m. q. 12 h] or aqueous potassium or sodium benzyl penicillin [22,000 to 44,000 iu/kg bwt i.v. q. 6 h]). Although often susceptible *in vitro* to trimethoprim sulfa, repeated failures *in vivo* have occurred (Verheyen *et al.* 2000). For horses that are refractory to twice daily i.m. injections, ceftiofur crystalline free acid (Excede)[1] is a useful option, although it provides more broad spectrum coverage than clinically needed. Chloramphenicol has been a useful oral option in horses in the need for extended treatments.

A short course (3–5 days) of penicillin has been effective during the acute phase of fever and depression to prevent abscessation, but these animals will not potentially develop immunity and are at risk of infection as soon as antibiotics are discontinued. Antibiotics are not recommended in horses with external abscesses as the treatment will prolong their maturation and resolution. Systemic antibiotics are indicated if these horses are concurrently anorexic, persistently febrile despite antipyretics, at risk of respiratory obstruction, or appear otherwise systemically affected. If rupture into the guttural pouch has occurred and aspiration of the mucopurulent discharge is possible, an extended course (10 days) of systemic penicillin is also warranted to prevent aspiration pneumonia and aid in the resolution of guttural pouch empyema. It has been argued that antimicrobial use after abscess development may lead to metastasis based on the theory that protein synthesis by the organism is changed by antimicrobial treatment and that a decreased immunogen level results in a suboptimal immune response. There are no experimental or clinical data to support such an occurrence, but treated horses are at high risk of infection after antibiotic discontinuation (Ramey 2007). There are also reports of outbreaks in which no antimicrobials were used and the incidence of complications was high (Sweeney *et al.* 1989; Spoormakers *et al.* 2003). Horses with complications such as purpura or metastatic abscessation definitely require the use of systemic antimicrobials for extended periods, the latter often requiring months of treatment. In cases with complications such as *S. equi* internal abdominal abscesses, the mean duration of treatment was 2 months in one study (Pusterla *et al.* 2007). Cases of purpura haemorrhagica also require the use of systemic corticosteroids (dexamethasone 0.1–0.2 mg/kg bwt i.v. or i.m. q. 12–24 h; prednisolone 0.5–1 mg/kg bwt *per os* q. 24 h) for an average of 3 weeks to reduce systemic vasculitis (Pusterla *et al.* 2003).

Treatment of carriers can vary depending on the situation. Many carriers identified at the end of an outbreak via active screening require only a topical gelatin/penicillin mixture (Sweeney *et al.* 2005) infused into the guttural pouches once free of visual empyema. Elimination of guttural pouch empyema requires repeated lavage (intensity varies depending on the severity) via polyethylene tubing through an endoscope, via a chambers catheter, or indwelling catheters into the guttural pouch (**Fig 8**) (Newton *et al.* 1997b). A total of 20% acetylcysteine in buffered saline solution (Bentz *et al.* 1996) have been added to lavages with success (although not always immediate). Long-standing carriers often have chondroids which are particularly difficult to remove, often requiring manual removal with endoscopic equipment such as a memory helical polyp retrieval basket (**Fig 9**) or surgical removal. Successful elimination of *S. equi* in these carriers requires local treatment of the guttural pouch with a gelatin/penicillin mixture after removal of the material within the guttural pouch (**Fig 10**). Repeated local treatment with concurrent systemic penicillin treatment for 10 days is necessary for refractory cases (Freeman 1980; Newton *et al.* 1997a).

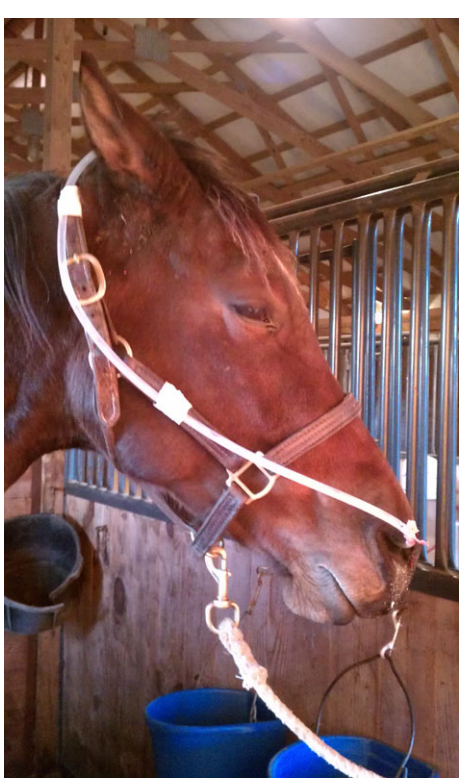

Fig 8: Embryo transfer catheter placed in the right guttural pouch of a horse with S. equi empyema.

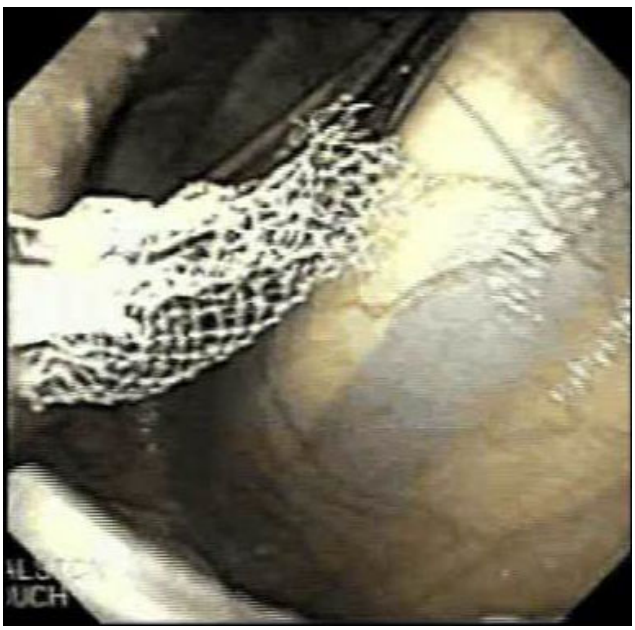

Fig 9: Helical polyp retrieval basket passed through a flexible endoscope in the guttural pouch of a horse with S. equi chondroids.

Fig 10: Infusion of penicillin antibiotic into the guttural pouch through tubing placed in the instrument channel of the flexible endoscope in a S. equi carrier.

Methods of outbreak control

Most outbreaks are thought to originate from introduction of an infected horse to a naïve population. All new horses should be isolated for 3 weeks and monitored for any signs of disease, including fever (>38.5°C or 101.3°F), or sudden increase in normally recorded biphasic temperatures. If cost is not prohibitive, horses should be screened for *S. equi* via guttural pouch endoscopy and lavage PCR and culture combination. If the animal is not previously vaccinated for *S. equi* and is located in a country that provides access to serology developed in the UK testing for both the *SEQ2190* and *SeM* genes, screening can be implemented as previously described in the section on serology (Robinson *et al.* 2013). Once an outbreak has occurred, twice daily monitoring of rectal temperatures of all horses on the farm is essential to contain the outbreak. Because febrile horses do not shed disease for the initial 2 days, immediate identification of febrile horses enables caretakers to isolate these horses before shedding occurs. Animals should be isolated based on the following categories: infected, contacts, recovered (but not yet tested for carrier status), recovered (and tested negative) and clean (unaffected). If any systemic antibiotics have been used at any time in the course of disease, these animals should not be reintroduced into an untested group of horses. All movement of horses to and from the farm should be stopped until they are determined to be noninfectious. All equipment (e.g. pitchforks, buckets, grooming tools) should also be segregated. Personnel handling infected horses should wear barrier precautions (i.e. gowns, gloves, plastic shoe covers) and, ideally, should not handle noninfected horses or should handle infected horses last. Water buckets should be disinfected daily. Facilities and equipment should be cleaned first to remove all organic material and then disinfected with phenols, iodophors, chlorhexidine compounds, bleach, or steam cleaned (Newton *et al.* 2000; Sweeney *et al.* 2005). Surfaces and equipment must be allowed to dry thoroughly. Ideally, paddocks that hold infected horses should be rested for at least 2 weeks. Recovery of the organism was not possible after 3 days on wooden fencing in 3 different outdoor environmental conditions using the less sensitive bacterial culture (Weese *et al.* 2009), but has been recovered for as long as 40–60 days on glass and wood, respectively in laboratory settings (Jorm 1992). If nasal discharge persists for longer than 2 weeks, guttural pouch endoscopy should be performed at that time. Since horses are known to typically shed *S. equi* for 2–3 weeks (and sometimes up to 6 weeks) (Sweeney *et al.* 2005), waiting a minimum of 4 weeks after the resolution of clinical signs has been recommended prior to performing guttural pouch endoscopy and testing. Guttural pouch lavage PCR and culture combination should be performed on the cases and their contacts to screen for carriers. One could argue that it is not practically and financially feasible to wait that long in an equine business operation so a cost analysis needs to be performed to determine whether earlier screening (which could result in treatment of more positives) outweighs waiting. A minimum recommended time to start guttural pouch screening is 2 weeks after the resolution of clinical signs. Going straight into the guttural pouches provides increased efficiency (both time and monetary) and sensitivity over 3 nasopharyngeal washes 3 weeks apart followed by guttural pouch endoscopy of the positives (**Fig 11**) (Boyle *et al.* 2015). If the outbreak is located in a country in which the combined *SeM* and *SEQ2190* serology is offered and the horses have no history of vaccination, then this serology can be used to identify seropositives in the contact population that need to scoped (Robinson *et al.* 2013; Waller 2014). Eradication of this disease will not be possible until carriers are eliminated.

Vaccination

A systemic extract vaccine (Strepvax II)[2] is available in the United States that is administered i.m. Historically, i.m. vaccines have tended to cause injection site reactions and are therefore not administered routinely. An intranasal

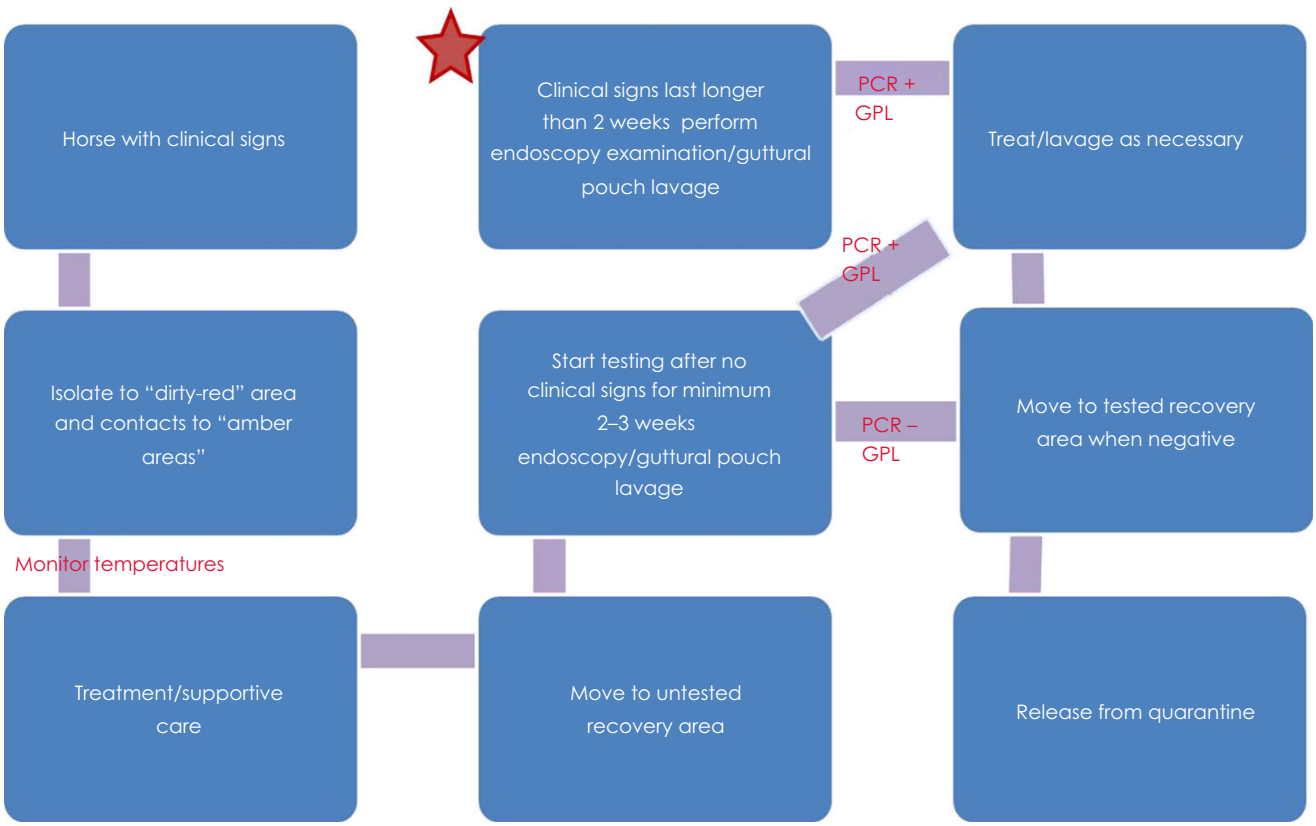

Fig 11: Flow chart of recommended steps in management of an outbreak of S. equi. Briefly, a horse or horses that present with clinical signs of strangles will be isolated to a 'dirty' or 'red' zone and all horses' contacts should be in placed in an 'amber' zone. Temperatures are monitored and any 'in contacts' are moved to the 'dirty' zone if the temperature is ≥101.3°F (38.5 °C). Supportive care and treatment of affected animals should be provided. Once clinical signs have resolved in affected horses, they are moved to a recovery area for untested horses. It is recommended that guttural pouch endoscopy and S. equi PCR and culture combination testing of the guttural pouch lavage (GPL) should start a minimum of 2–3 weeks after the resolution of clinical signs. If the horse is positive on GPL or has an abnormal endoscopy, copiously lavage the guttural pouch and treat with topical and possibly systemic antibiotics. If the GPL is negative, then move the horse to a tested recovery area (green). If a horse remains clinical for longer than 2 weeks, perform a guttural pouch examination at that time to determine if the horse has significant empyema and requires lavage to remove physical contamination of the pouch in order to shorten time to resolution.

vaccine (Pinnacle IN)[1] is also available and contains an attenuated live strain of *S. equi* subsp *equi* that is antigenic with low pathogenicity. In Europe, a modified live submucosal vaccine (Equilis StrepE)[3] is available, labelled for 3 months of immunity and has been shown to be safe in pregnant mares (Reinhold and Venner 2010). The immunity level provided by these vaccines is lower than that produced during recovery of natural disease. Due to potential complications associated with strangles vaccines, advisement of vaccination is based on a risk assessment of the case (Sweeney *et al.* 2005). Experimental models performed by the manufacture of the intranasal vaccine have shown a more significant reduction of clinical disease with the use of the intranasal vaccine than use of the i.m. vaccines, suggesting that Pinnacle IN[1] is the more effective vaccine (Wilson 2005). Complications associated with the intranasal vaccine include mild clinical signs such as coughing and nasal discharge for a few days after vaccination to significant pharyngitis. *Streptococcus equi* abscessation at the site of other i.m. vaccines given concurrently with intranasal strangles vaccines can occur if not handled separately. Vaccination with the intranasal vaccine is not recommended to cases under a year of age due to the risk of significant clinical disease (fevers and mandibular/retropharyngeal lymph node enlargement) and increased shedding of the vaccine strain (Borst *et al.* 2011). The intranasal vaccine should also not be given concurrently with other invasive procedures such as joint injections and surgeries such as routine castrations. Severe, life-threatening complications such as purpura haemorrhagica have been associated with 2 of the 3 vaccines (Strepvax II[2] and Pinnacle IN[1]) (Timoney 1999; Pusterla *et al.* 2003). Vaccination during or within a year of an outbreak is not recommended with these 2 vaccines (Boyle *et al.* 2012b). Safety of the Equilis StrepE vaccine during an outbreak has not been tested. Timoney and others (Sweeney *et al.* 2005) have suggested that horses with high SeM-specific serum antibody titres (≥3200) may be predisposed to purpura when vaccinated for *S. equi* with the attenuated-live intranasal *S equi* vaccine. If vaccination is deemed necessary within 2 years of an outbreak, a SeM ELISA should be obtained prior to administration (Boyle *et al.* 2012b).

Future directions/research

Strangles is a highly contagious upper respiratory disease that persists in nature due to the presence of silent carriers.

Improved diagnostics are needed to detect infection earlier, more conveniently and at less cost. Stall-side detection would accelerate identification of affected horses, which in turn would lead to faster quarantine protocols and less spread of disease. Loop-mediated isothermal amplification (LAMP) technology can identify DNA without the use of heat cycling and has been investigated for the detection of *S. equi* (North *et al.* 2012; Boyle *et al.* 2015). Researchers are also working to improve vaccination for *S. equi* (Rodrigues *et al.* 2012; Waller 2014; Robinson *et al.* 2015).

Author's declaration of interests

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Ethical animal research

Ethical review not applicable for this review article.

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Manufacturers' addresses

[1]Zoetis, New Jersey, USA.
[2]Boehringer Ingelheim Pharmaceuticals Inc, Ridgefield, Connecticut, USA.
[3]MSD Animal Health, Walton, Milton Keynes, Bucks, UK.

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Supporting information

Additional Supporting Information may be found in the online version of this article at the publisher's website:

Supplementary Item 1: Video of guttural pouch empyema.