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MANAGEMENT OF INFECTED JOINTS AND TENDON SHEATHS IN HORSES.

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Synovial infections in horses include infectious arthritis, infectious tenosynovitis and infectious bursitis. Early diagnosis and treatment of those synovial infections is very important to guarantee a successful outcome.

Synovial infection produces the classical signs of inflammation around the joint or tendon sheath. These include heat, painful periarticular swelling and oedema, distension of the joint, erythema of the surrounding skin and pain on pressure and flexion. Lameness is often very severe/non-weight bearing. In some cases the lameness is less severe if the infection is seen early in the disease process, if analgesics have been administered (systemic NSAID or corticosteroids intra articular) or if a larger wound is present which allows easy drainage of synovial fluid (less pressure in the joint).

In some cases it is very difficult to differentiate an acute traumatic joint injury from an early septic joint. Because synovial infection often leads to permanent lameness early recognition of an infection and appropriate treatment with a sensitive antibiotic is paramount. Repeated synovial fluid analysis are very helpful in monitoring the response to treatment and isolation of microorganisms by culturing will help the clinician in deciding which antibiotic to use.

However there are a few problems encountered in isolating micro-organism from a joint:
- Synovial fluid cultures in horses with suspected infectious synovitis may yield (false) negative results in up to 27% (Schneider et al, 1992) to 45% (Madison et al, 1991) of cases.
- The accuracy of a standard agar plate method to detect bacterial growth is not high.
- Synovial fluid cultures can be negative after a couple of days of antibiotic treatment (systemically and/or intra articular).
- Collecting synovial fluid is not always possible especially in cases where synovial fluid can drain out of the joint (e.g. through a wound).
- Care should be taken during the sampling to avoid iatrogenic contamination of the synovial fluid sample.
- Synovial fluid cultures may take up to 7-10 days before having a result. Meanwhile a treatment should be ongoing.

Another important issue to deal with is the permanent thickening and fibrosis of the fibrous part of the joint capsule. This will often lead to permanent joint dysfunction also in absence of infection. Early treatment with steroidal drug is very tempting to reduce this capsulitis and reduced joint motion but one has to be sure that the infection is under control.

During the talk those problems will be discussed together with some research result of Pille F. et al, 2004 using PCR (polymerase chain reaction) techniques to detect bacterial DNA directly from clinical samples of synovial fluid of horse suspected of infectious synovitis.

Aetiology:
The four most common causes of joint infection in horses are articular wounds (24%), intra synovial injections (22%), post-surgical infection (13%), haematogenous localization (17 to 34%) and idiopathic causes (6%) (Schneider et al, 1992). In foals younger than 4 months old a haematogenous spread of bacteria resulting in (poly)arthritis and/or (poly)osteomyelitis is common in the presence of general infections and/or in foals with hypogammaglobulinemia (failure of passive transfer). Rarely, joint infections are associated with extension of cellulites.

Staphylococcus and most frequently S. Aureus is isolated from infected joints of adult horses but the presence will vary with the practice location and the distribution of the equine caseload. In a study performed by Schneider et al 1992, staphylococcus was often isolated in cases of iatrogenic infection (post intra articular injection or surgery). Enterobacteriaceae were often isolated after penetrating wounds. Multibacterial infection is often found in foals suffering
from poly-arthritis with Escherichia Coli being commonly present. Anaerobic organisms were isolated in 10% of all equine cases. Mycotic arthritis is not common. Candida species (Rilet et al, 1992; Madison et al; 1995) and Scedosporium species (Swerczek et al, 2001) are described.

**Diagnosis:**

Symptoms of synovial infection are very similar to those of acute non-infected synovitis. Making a correct diagnosis can be a challenge in absence of a visible peri-articular wound. Horses with an infected joint are often very lame. If a (puncture) wound is present over a joint or tendon sheath and the horse is obviously lame (lame at the walk) a diagnosis of suspected joint infection should be made. The horse should be examined and treated as if an infected joint/tendon sheath is present until the contrary is proven. Absence of severe lameness does not exclude infection of the joint. If drainage of synovial fluid if possible from the joint, lameness can be very minimal in the early days. Intra articular medication or NSAID systemically can mask the lameness and post pone the diagnosis of infection. Intra-synovial corticosteroids can delay symptoms of infection up to 7-10 days (personal observation).

Drainage of synovial fluid from the (puncture) wound is often not present. Fibrin will often seal the wound in the synovial membrane. A strong fibrin clot can even prevent outflow of saline injected in the joint under pressure when checking for joint penetrations.

In foals infected joints should be differentiated from immune mediated polysynovitis and reactive arthritis. In those foals virtually all cases are associated with Rhodococcus infection. In foals with polyarthritis the presence of hypoglobulinemia should always be checked.

Radiography is of little value in adult horses. Osteomyelitis is uncommon and radiographic signs of degenerative joint disease take many weeks to months to develop. The major value of radiographic examination in adults lays in examining the joint for bone fragments and presence of foreign bodies. In foals radiography is always indicated. Osteomyelitis and changes in the epi-or metaphysis are often present after 1 week.

Ultrasonography of the joint is helpful to diagnose joint distension (not always easy to see with the concurrent peri-articular inflammatory oedema) and the presence of fibrin in the joint. It is also particularly helpful in the diagnosis of infection and joint distension in the upper limb joint (shoulder, bicipital bursa, hip) that are not readily palpable.

Aseptic arthrocentesis of the affected joint and synovial fluid analysis and synovial fluid culture is the best way to reach a diagnosis. Arthrocentesis should be performed away from the site of possible infection. Synovial fluid should be grossly observed for colour and clarity and submitted for WBC count, differential count and total protein level. Synovial fluid can changes in a turbid dark yellow fluid with some fibrin clots within a couple of hours after inoculation of bacteria. In cases were aspiration of fluid is not possible due to open drainage and/or presence of too much fibrin, a good quantity of saline should be injected and partially retrieved. This sample can than be used for bacteriological evaluation.

Normal synovial fluid contains ± 770 ± 73 WBC/mm3 and 7.87-± 0.03g/l total protein. Twenty four hours after experimental inoculation of the hock joint with bacteria the WBC count raises up to 40,000 to 70,000 WBC/mm3, mainly neutrophils (> 90%) and the total protein increased up to 46-58 g/l (Tulama et al, 1989).

In equine joint infections, cell counts of ≥ 30,000 WBC/mm3, neutrophils of > 80% and total protein of 40 g/l are strongly indicative of infection (Bertone, 1996). WBC counts of 47,000 to 180,000 wbc/mm3 and neutrophils of > 90% are often found in clinical cases of joint infection. In chronic cases of infection WBC count can be as low as 5000 -10.000 wbc/mm3 but the total protein level remains high (> 50 g/l) (Bertone, 1996).

In cases of non-infectious traumatic synovitis WBC count can also raise up to 50,000 WBC/mm3 but neutrophils level remains generally lower than 80% and total protein lower than 30 g/l. However there is a grey zone between inflamed non-infected synovial fluid and clearly infected synovial fluid, which makes it difficult to decide if the joint needs flushing and/or antimicrobial treatment and/or cortico-steroid treatment.

To be successful in identifying a microorganism from a suspected infected synovial cavity a synovial fluid culture should be performed. The best way to perform this is by using blood culture methods. Synovial fluid (up to 5 ml) should be aspirated aseptically and inoculated in a blood
Culture bottle. Strict asepsis is mandatory. The culture bottles are incubated and plated. Culture bottles offer the advantage of convenience, enhancing organism proliferation with ideal media, diluting antimicrobial substances, containing inhibitors of antibiotics, and allow a larger volume of fluid to be inoculated (Bertone et al, 1987 and Montgomery et al, 1989). Bottles should be cultured aerobically and anaerobically and an antibiogram should be obtained if bacteria are isolated.

Culturing organism of the synovial membrane is not as successful as cultures of the synovial fluid. Madison et al, 1991 obtained positive cultures from 52% of synovial fluid samples and 36% of synovial membrane cultures.

Synovial histology seems to have little diagnostic value (Madison et al, 1991). Pille et al, 2004 described the use of broad range 16S rRNA gene PCR and compared the results with agar plate methods and blood culture methods. The study included 57 synovial fluid samples of horses with presumed synovial infection and a large control group consisting of 31 synovial fluid samples originating from clinical normal horses and horses with aseptic synovial inflammation. Polymerase chain reaction (PCR) techniques detect the presence of bacterial DNA in synovial fluid samples. The technique is more time consuming than culture techniques, require absolute asepsis to prevent contamination and false positive results but results are already obtained after 48h. They concluded that PCR had a superior detection rate (89.5%) to other detection methods. Bacterial isolation using blood culture had a highly acceptable detection rate of 77.6%. Agar plate had a very low sensitivity of 37.8%. The highest sensitivity (91.8%) for the detection of synovial infection was achieved when the results of blood culture and 16S PCR were combined.

The potential power of bacterial PCR lies in the detection of synovial infections caused by microorganisms that are difficult to culture or in patients that had antibiotic treatment. Synovial fluid aspirates become negative 2-3 days after initiation of antibiotics but with PCR, bacterial DNA can be demonstrated up to 22 days (Canvin et al, 1997; Van der heijden et al, 1999). PCR also has the potential to confirm the absence of bacterial DNA after treatment with antibiotics, which may limit the duration of antibiotic treatment and deviate therapeutic efforts to the reduction of synovial inflammation often debilitating the horse for the rest of his career. There are several reports describing the detection of bacterial DNA in human patients with non-infectious inflammatory joint diseases (rheumatoid arthritis, crystal induced arthritis, reactive arthritis) but no report are published on this topic in non-infectious joint diseases in horses. Reactive arthritis in horses is uncommon and virtually all cases published are associated with Rhodococcus equi and immune-mediated arthritis. The disadvantage of the technique is the fact that no susceptibility patterns can be obtained from the isolated bacteria. A combination of PCR with blood culture technique remains essential.

Treatment:

First of all prevention is important. A contaminated joint is not in infected joint and one should aim to keep it that way. If a contaminated joint (often associated with wounds) is correctly treated within the 24h (antibiotics, lavage) the chance of developing infection is low.

Early recognition and early treatment is the key to success. Treatment including joint lavage should be performed within the 24 h but preferably within the 8 hours after inoculation of the joint (personal observation).

Iatrogenic infections after synovial injections are still routinely presented to our hospital (± 5 cases a year). They are often referred 3-10 days after injection and the outcome (e.g. return to original level of use) is often poor. Those horses are often treated with corticosteroids and infection is often the result of insufficient asepsis prior to arthrocentesis (improper scrubbing or bad injections techniques). Hague et al (1997) concluded that aseptic preparation of the skin could be accomplished without removing the hair. The presence of hair is not important but the duration of the povidone scrub is important. In foals suffering from hypogammaglobulinemia a plasma-transfusion should be performed as soon as possible to reduce the chance of infectious polyarthritis.
Surgical treatment:

It is well recognised that joint drainage is an essential part of the treatment. The most commonly recommended technique is arthroscopic lavage. After this the surgeon can decide to close the arthroscopy portals or to leave them open to allow for permanent drainage underneath a sterile bandage. Arthroscopy offers the advantage of superior visualisation and removal of fibrin and synovial proliferations present in the joint. Foreign material can also be recognised and removed. Lavage should be performed with large volumes (3-9 L) of Na Cl 0.9% or lactated ringers. The use of antiseptics in low concentrations (chlorhexidine, Povidone) and the use of antibiotics in the lavage fluid are not recommended, as they will not influence the end results. Dimethylsulfoxide (10-40%) can be added in the last lavage (Bertone, 1999) but its use remains a subject of debate (Welch et al, 1991; Adair et al, 1991; Matthews et al, 1998; Smith et al, 2000).

If lavage is performed through needles, large diameter needles should be used (3-4 mm). The needles should be positioned in different locations to allow maximum cleaning of the joint. Both dorsal and palmar/plantar pouches should be flushed. It is also advisable to position the leg in both flexion and extension during the procedure.

The day after the joint lavage analysis of the joint fluid (WBC count + total protein) should be performed. In some cases several joint lavages are necessary. In general the joint is lavaged every 2 days until the WBC count of the synovial fluid drops underneath 15.000/mm3 (Bertone, 1999; Meijer et al, 2000). Daily intra articular treatment with antibiotics is strongly advised until the infection is under control (see local antibiotic treatment). In unresponsive cases, usually cases with lots of fibrin formation, arthroscope portals are left open. This continues drainage allows decompression of the synovial cavity, which will decrease inflammatory response and pain in the affected joint. In some cases an indwelling drain can be positioned in the joint, which allows for daily postoperative lavage of the synovial cavity even in the standing horse. Ascending infections are always a risk when using intra articular drains or when small arthrotomy wounds are left open. Careful sterile bandaging is mandatory. In proximal located joints bandaging is not possible (e.g. stifles joint). In those cases the horse should be attached to prevent them of lying down.

Surgical arthrodesis of the joint is an option in some joints (pastern joint, fetlock joint, tarsal joints) where joint infection affected cartilage and/or subchondral bone to such an extend that joint function is permanently lost (Steenhaut et al, 1985; Gibson et al, 1989; Honnas et al, 1992; Groom et al, 2000).

Local antibiotics

Antibiotic therapy is a critical component of the treatment of infectious arthritis and has been shown in horses to reduce systemic signs of infection and inflammation (Bertone et al, 1987). Intrasyovial administration of antibiotics in a joint, tendon sheath or bursa after surgical treatment, is almost always part of the standard treatment regime. Only non-irritating antibiotics such as gentamycine, amikacine, sodiumpenicilline, cefazoline and ceftiofur are used (Kent Lloyd et al, 1988; Mills et al, 2000; Ducharme NG and Mitchell L, 2004). If possible their use should be based on the results of an antibiogram. Daily postoperative intra-synovial treatment is recommended in those horses that are still visibly lame at the walk the day after surgery and/or when the WBC count of the synovial fluid remains > 20.000 /mm3.

Regional IV perfusion of joints is an effective way to deliver high concentrations of antibiotics, particularly to ischemic tissue (Whitehair KJ et al, 1992). High concentrations of antibiotics are found both intra- and peri-synovial (Whitehair KJ et al, 1992; Murphey et al, 1999). This technique is easy to apply, even on the standing horse, for treatment of synovial infections distal to the elbow and stifle joint. A tourniquet is wrapped proximal to the affected joint or tendon sheath to occlude superficial vasculature and an antibiotic is injected into a vein distal to the site of infection. Gentamycine, amikacine, cefazoline and ceftiofur have been used successfully. Enrofloxacine is not recommended for intravenous regional perfusion as it can cause an important local irritation with subsequent skin necrosis. The antibiotic used is diluted in 30-60 ml of sterile saline and injected through a 20 gauge butterfly catheter. The tourniquet is left in place for 20-30 minutes. The tourniquet is than removed, followed by the catheter and a pressure bandage is applied over the catheter site.
Intraosseus perfusion can be used to deliver high concentrations of antibiotics in joints and bones distal to the site of injection (Mattson S et al, 2004). A tourniquet is placed proximal to the intended site. A 4 mm unicortical hole is drilled through the cortex and a 5.5 cannulated bone screw with luer lock adaptor is inserted with pliers. Five ml of local anaesthetic is injected followed by the selected antibiotic (gentamycine 2.2 mg/kg) diluted in 30-60 ml of sterile saline. The tourniquet is removed after 30 minutes. A sterile bandage is applied. An intraosseus screw allows for daily local perfusion without the problems of venous thrombosis, which can occur, rapidly with regional perfusion.

Gentamycine impregnated polymethylmethacrylate beads can be implanted in a joint or tendon sheath through a small arthrotomy wound (Bertone, 1999, Booth et al, 2001; Holcombe et al, 1997; Ethell et al, 2000). They release gentamycin continuously, which will lead to high intrasynovial concentrations. PMMA beads are non absorbable and have to be removed. Biodegradable hydroxyapatite cement is used (Ethell et al, 2000) together with several antibiotics (amikacine, gentamycine, ciprofloxacin, cefazolin, ceftiofur, ticarcillin, vancomycin) (Ducharme NG and Mitchell L, 2004). Biodegradables are effective in vitro but more expensive.

Systemic antimicrobial therapy

Systemically administration of antibiotics is also an essential part of the treatment. In general antibiotics are administered for several weeks. Intravenous administration of antibiotics is preferably the first 5-7 days. In general, the treatment is started with a broad-spectrum antibiotic. The antibiotic used can be changed after receiving the antibiogram results from the synovial fluid if necessary. Oral treatment is only advised once any infection is controlled. Gentamycine, amikacine, Na-Penicillin, amoxicilline-clavulanic acid, ceftiofur and enrofloxacine are commonly used. Trimethoprim-sulfonamides are more commonly used as an "after infection treatment". Once the infection is considered eliminated systemic antibiotics should be continued for 1-2 weeks. Trimethoprim-sulfonamides can than be used orally at a rate of 30 mg/kg BID. The same dose rate once a day is not effective (Bertone et al, 1988).

The use of insufficient doses of antibiotic is a common error in the treatment of infection in horses. Ceftiofur at 2.2 mg/kg BID will result in an effective (>MIC) concentration for only 12 h. (Pille et al, 2004). An adult horse of 450 kg needs 3-6 gr ceftiofur IV per day to maintain effective (>MIC) concentrations (Mills et al, 2000).

See table below for the dosages of antibiotics currently used to treat infectious synovial cavities in horses.

**NSAID**

The use of NSAID is almost always indicated in the management of equine synovial infections. NSAID will suppress prostaglandin production and joint inflammation. The also reduce pain and lameness. One should be careful not to use to high concentrations of NSAID. It will mask the lameness and this will make it impossible to assess the effect of the treatment (joint lavage + antimicrobial treatment). Low dose of NSAID such as phenylbutazone (2.2 mg/kg is a half dose) should be administered only once daily and lameness can be assessed just before treatment. Reduction of pain however is very important to a successful outcome because of the risk of contra lateral laminitis.

Morphine (80 to 120 microgram/kg IM, SID-QID) can effectively control the pain during the first days of treatment.

The use of corticosteroids, as a part of treatment of synovial infections, remains controversial. Its use to reduce permanent periarticular fibrosis and joint stiffening is very tempting. Meijer et al (2000) used routinely 4-8 mg dexamethasone intra articular once the bacteriology was negative and the WBC count of the synovial fluid was lower than 15.000/mm3.

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<table>
<thead>
<tr>
<th>Antibiotics</th>
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<tbody>
<tr>
<td>Gentamycine</td>
</tr>
<tr>
<td>Amikacine</td>
</tr>
<tr>
<td>Na-Penicillin</td>
</tr>
<tr>
<td>Amoxicilline-clavulamic acid</td>
</tr>
<tr>
<td>Cefazolin</td>
</tr>
<tr>
<td>Ceftiofur</td>
</tr>
<tr>
<td>Ticarcillin</td>
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<tr>
<td>Vancomycin</td>
</tr>
<tr>
<td>Trimethoprim-sulfonamides</td>
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</tbody>
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<table>
<thead>
<tr>
<th>NSAID</th>
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</thead>
<tbody>
<tr>
<td>Phenylbutazone</td>
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<tr>
<td>Morphine</td>
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</table>

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**Prognosis**


Horses that are sound at the walk the day after the first joint lavage (receiving not more than 2.2 mg/kg phenylbutazone) have a reasonable good chance of full recovery (personal observations).

The majority of these cases are patients that have been treated within the 24 h after injury probably with a contaminated joint and not yet an infected joint. Once the infection is well established the prognosis for return to previous level of work is guarded to poor.

Wright et al, 1999 reported a 62.5 % recovery rate after arthroscopical lavage of the navicular bursa in 16 cases.

Pille et al, 2004 reported a 72% recovery rate after needle lavage combined with regional IV perfusion.

### Systemic antibiotics commonly used in horses with contaminated and infected synovial cavities

<table>
<thead>
<tr>
<th>Drug</th>
<th>Route</th>
<th>Dose</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amikacin</td>
<td>IV or IM</td>
<td>15 mg/kg q 24 h</td>
<td>Foal</td>
</tr>
<tr>
<td>Amoxicillin-clavulanic acid</td>
<td>IV or IM</td>
<td>15 mg/kg q 8 h</td>
<td>Foals</td>
</tr>
<tr>
<td>Ceftiofur</td>
<td>IV or IM</td>
<td>2.2 mg/kg q 12 h</td>
<td>-</td>
</tr>
<tr>
<td>Enrofloxacin</td>
<td>IV</td>
<td>5 mg/kg q 24 h</td>
<td>Bone infection</td>
</tr>
<tr>
<td></td>
<td>Oral</td>
<td>7.5 mg/kg q 24 h</td>
<td>Bone infection</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>Oral</td>
<td>25 mg/kg q 8 h</td>
<td>Foals R. Equi</td>
</tr>
<tr>
<td>Gentamycin</td>
<td>IV</td>
<td>6.6 mg/kg q 24 h</td>
<td>-</td>
</tr>
<tr>
<td>Oxytetracycline</td>
<td>IV</td>
<td>5 mg/kg q 12 h</td>
<td>Bone infection</td>
</tr>
<tr>
<td>Procaine Penicillin</td>
<td>IM</td>
<td>20,000 IU/kg q 12 h</td>
<td>-</td>
</tr>
<tr>
<td>Rifampin</td>
<td>Oral</td>
<td>20 mg/kg q 24 h</td>
<td>Foals R. Equi</td>
</tr>
<tr>
<td>Sodium Penicillin</td>
<td>IV</td>
<td>20,000 IU/Kg q 6-8 h</td>
<td>-</td>
</tr>
<tr>
<td>Trimethoprim-sulfa</td>
<td>Oral</td>
<td>30 mg/kg q 12 h</td>
<td>-</td>
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