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Synovial structures – to treat or not to treat?

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Introduction

Septic arthritis is the most common infection of synovial structures in cattle ¹, followed by infection of tendon sheaths and synovial bursae ^{2,3}. Synovial infection is a severe disease that without adequate therapy determines the use and the life of the affected animal, either by progressive joint destruction or expanding to systemic sepsis.

Septic arthritis and tenosynovitis is defined as an inflammatory condition caused by invasion of microorganisms into the synovial space. An immunosuppression ⁴ often accompanies joint infection which makes treatment especially difficult. Most commonly septic arthritis is caused by bacteria, but other microorganisms (virus, fungi, protozoan) are not ruled out with the current standard diagnostic work up. Commonly isolated bacteria are *A. pyogenes*, Streptococci, Staphylococci, *E. coli*, *Bacteroides* sp.

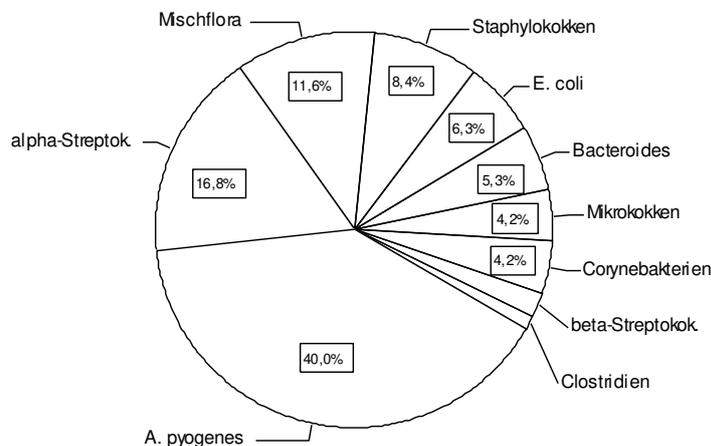


Fig. 1 Isolation of bacteria from septic joints (75 positive/118) of cattle ⁵.

There are several possible routes of infection. In cattle, haematogenous spread was found to be the most common in adult cattle and calves (57%), followed by indirect infection from a focus nearby (31%). Direct infection through trauma or arthrocentesis was the least common (12%). Frequently diagnosed sources of infection in adult cows are diseases originating in the postpartum period (lacerations after forced extraction, retained placenta, endometritis, mastitis, and endocarditis). In a larger study ⁵ concomitant orthopaedic diseases like phlegmons, wounds, bursitis, claw diseases and decubital ulcers were found in more than half of dairy cows presented with septic arthritis. In calves, umbilical remnant infection, pneumonia, and diarrhoea, often associated with failure of passive transfer, were present.

Despite haematogenous spread being the most common way of infection, usually only one joint is infected, and polyarthritis is rare, except in young calves. In calves, polyarthritis is seen more commonly than in adult cattle ⁶. When several cows in a herd develop polyarthritis, examination for infectious agents (*Mycoplasma* spp. *Brucella*, *Chlamydia* spp.) should be initiated ⁷.

After the infectious agent has entered the synovial space, a severe inflammatory response develops. Bacteria damage the cartilage, the synovial membrane directly and alter the character of the synovial fluid. Even more severe for articular degeneration is the immunological host response. The articular cartilage undergoes degeneration due to inadequate nutrition and enzymatic degradation, which results in break-down products, which in turn cause synovitis, making the vicious circle complete (Martens and Auer 1980).

Diagnosis

For successful treatment of septic arthritis, early diagnosis is essential. If a septic arthritis is not recognized and treated as such at the earliest possible stage, prognosis becomes less favourable. A false negative diagnosis might even terminate the animal's life. On the other hand, a false positive diagnosis induces an unnecessary and expensive treatment and causes withdrawal times on milk and meat⁸. Because no gold standard for diagnosis exists, a combination of clinical findings, radiographic examination, synovial fluid analysis and microbial culture results are necessary to establish a diagnosis⁵.

A thorough clinical exam with special emphasis to identify the possible cause for the septic joint (adults: decubital ulcers, puerperal problems, calves: umbilicus, pneumonia, diarrhea, failure of passive immunotransfer) should be performed as always. With a wound in the joint region septic arthritis should be suspected and always ruled out by arthrocentesis and flushing the joint from a point distant to the wound.

The most important clinical signs in the early stage are lameness, joint effusion, pain on palpation and during passive motion of the affected joint. The animal can be febrile and depressed. But absence of elevated temperature or reduced food intake and altered behaviour does not rule out septic arthritis.

If a swollen joint is found in a lame cow, arthrocentesis should be performed after strict aseptic preparation of the site, for macroscopic and microscopic evaluation of the synovial fluid and bacterial culture. Macroscopic aspects for infected synovia are: higher volume, reduced viscosity, changed colour (yellow, reddish, brown), turbidity, fibrin, and abnormal odour in putrid arthritis.

White blood cell count (WBC), percentages of neutrophils (PMN), total protein (TP) concentration and specific gravity are standard parameters in synovial fluid analysis. TP concentration > 4.5 g/dl, WBC $\geq 25'000$ cells/ μ l, percentage of PMN $\geq 80\%$ indicate septic arthritis. These variables should be used as positive predictive values⁶. Lower values of these parameters do not exclude the presence of bacteria. WBC count varies widely in septic arthritis, even in synovial fluid with counts as low as 2800 cells/ μ l positive cultures were found, indicating that it lacks sensitivity as cut-off data without cell differential⁵.

It is not uncommon to have negative bacteriological cultures of synovial fluid that corresponds with all signs of septic arthritis. Positive bacteriological cultures are reported with 50-70%. The simultaneous use of different culture mediums (without medium, transport medium and blood culture) increased the chance for positive results, however no medium was found to be superior to the other⁵.

Radiographic findings are soft tissue swelling, gas accumulation in the joint, widening of the joint space in acute condition or narrowing of the joint space because of articular destruction. Bony lesions, in cattle mainly osteolytic changes, are seen if at least 40 % of the mineralized bone matrix is removed (10-14days after onset of infection). Because chronic presentation is common in food animals, radiologic changes are often obvious. Management and the slow gait of adult cattle are mentioned as reasons why owners and veterinarians lacking expertise in this field do not recognize lameness in the early stage^{9,10}.

Ultrasound is superior to radiography for evaluation of soft tissues. Synovial fluid and membrane, the joint surface and surrounding connective tissues can be evaluated within certain limits¹¹.

General principles of treatment with emphasis on joints

The ideal treatment of synovial infection is still subject of discussion in veterinary as well as in humane medicine. The following points are the aims of a treatment.

- 1) Control the infection
- 2) Remove bacteria
- 3) Remove abnormal joint fluid
- 4) Control inflammation
- 5) Restore joint function

Ad 1: Antibiotics

To control the infection, antibiotics should be administered at the earliest possible time. Until results of the microbiological culture are available, treatment should be initiated with broad spectrum antibiotics. Cephalosporins, ampicillin or penicillin in combination gentamicin are a good choice. A high percentage of bacteria (> 30 %) showed in-vitro-resistance to tetracycline and sulphonamides⁵. These antibiotics – although cheap – should therefore not be used routinely as first choice. IV or IM administration should be preferred to reach higher local minimal inhibitory concentration levels. In general, most antibiotics diffuse into a healthy synovial cavity. However pharmacokinetics are different in the septic joint because of the higher intrasynovial pressure, periarticular oedema, presence of fibrin and the lower pH. Nuss (2000) showed that the percentage of positive microbial culture was independent of pre-treatment, which supports the hypothesis that systemically administered antibiotics do not reach MIC in septic joints without further invasive treatment steps.

Intraarticular administration of antibiotics was controversy discussed because it can induce a chemical synovitis. Intraarticular gentamicin reaches antibiotic concentrations in the synovial fluid above the minimal inhibitory concentrations for 24h and causes only a mild synovitis (Lloyd et al. 1990).

Further positive aspects of local antibiotic treatment are less systemic side effects, lower amount of drugs needed and thus lower costs. Disadvantages are necessity for repeated arthrocentesis for administration which however can be used for cell count and other synovial diagnostic measures. Dosage recommendation for intra articular administration of gentamicin is 400-800mg per joint, but should not exceed a single systemic body weight dose daily. Alternatively, a dose of 150mg of ceftiofur is recommended on an empirical basis. Clinicians must be aware that intra articular administration may be extra-label use of antibiotics.

Further options for local antibiotic treatment are regional intravenous or intraosseous limb perfusion, impregnated PMMA-beads, gentamicin impregnated collagen sponges or microsphere application in the future. The primary disease if found should be treated as aggressive as possible. An infected umbilicus in a calf with septic arthritis should be surgically removed. In calves with suspected failure of passive transfer blood or plasma should be transfused. Systemic antibiotics should be administered for 2-3 weeks after improvement of clinical signs.

Ad 1, 2 and 3: Lavage of synovial structures

Aspiration, distension- or through and through lavage, arthroscopy or arthrotomy are used to remove debris and altered joint fluid. In veterinary medicine lavage is stated as superior to aspiration in removing inflammatory products. Distension irrigation, with aspiration and irrigation through the same needle, creates turbulence and dislodges the debris possibly better than through-and-through-lavage in small joints like hip or shoulder¹². For through and through lavage, two or several needles are placed in different joint pouches as far away from each other as possible. Thus, larger amounts of fluids can be flushed through the joint. If the needles are blocked alternating to distend the joint, it has similar effects as tidal lavage (distension-irrigation). With both forms of irrigation the joint is flushed until the returning fluid is clear.

As lavage solutions, ringers' solution or lactated ringer solution are recommended. Joint lavage should be accomplished with adequate restraint, sedation and intraarticular anaesthesia and/or nerve blocks. If the initial therapy is not successful, further therapeutic steps are indicated. The clinical presentation (lameness) of the patient should improve within 2-3 days after lavage, the total cell count should decrease. Is this is the case, lavage can be repeated every other day until the patient is sound and the total cell count is below 15'000cells/ μ l¹³.

Ad 1, 2 and 3: Arthroscopy/Tenosynovioscopy

Arthroscopy and tenosynovioscopy provides the advantages of lavage under visual control, and to assess the soft tissues and the cartilage. Debris and fibrin clots can be removed with rasping instruments, and lytic bony areas curetted. In bovine medicine only few reports exist about its use. Reasons for limited use are higher costs of instrumentation, the need for general anaesthesia and poor visibility of structures because of fibrin accumulation in the synovial cavity.

Ad 1, 2 and 3: Arthrotomy

The approaches to the joint are the same for arthrotomy and arthroscopy, with the difference that they are elongated for arthrotomy to enable digital or visual exploration. In joints distal to the elbow/stifle arthrotomy can be accomplished under local anaesthesia (nerve blocks, RIVA). After arthrotomy, the incision sites can be primarily closed or left to heal by second intention to drain the joint. The later bears the risk of ascending infection.

The decision for conservative (lavage) or surgical (arthrotomy or arthroscopy) treatment should be based on the stage of arthritis/tenosynovitis. In mild (serous to serofibrinous) synovial infection lavage therapy shows good success rates, whereas in severe arthritis (fibrinous, purulent or putrid) success rates are better if surgical treatment is chosen as the initial treatment^{5,12}.

If the clinical presentation does not improve, or the cell count does not decrease after two lavages, or if the needles tend to get blocked with fibrin, surgical treatment should be initiated.

Ad 1, 2, and 3: Facilitated ankylosis

Facilitated ankylosis after removal of all infected tissue is the final solution if chronicity of the disease prevents restoration of joint function or when no treatment was effective. Ankylosis of articulation of the distal limb does not interfere with normal use of the animal, whereas with ankylosis of high motion joints, such as carpus and tarsus, the animal must be kept in a box or small pasture.

Ad 4 and 5: Control of inflammation and function

Antibiotic treatment and removal of altered joint fluid are the most important approach to control inflammation. Additionally NSAIDs should be given to reduce inflammation response and increase the comfort of the patient. The NSAID Ketoprofen was shown to improve gait in lame cows, and is licensed for use in dairy cows with short or even no milk withdrawal. If prolonged administration is necessary especially calves should be monitored for abomasal ulcers.

The cartilage of the affected joint is prone to injuries, especially in the weight bearing surface. Thus, exercise should be restricted to a minimum. The patient should be kept in a box/tie stall with comfortable, dry bedding. In joints distal to the elbow and stifle, heavy bandages, splints or cast can be applied to minimize motion and support healing. This further reduces pain caused by accidental joint movements. In front limbs, full limb cast/splints are generally tolerated well. In hind limbs especially heavy animals may be hindered by full limb splints/cast. In these cases, the positive effects and risks of fixation (rupture of the *musculus fibularis tertius*) have to be calculated.

Prognosis

Reasons for therapeutic failure are based on the problem to eliminate infection¹⁴ or problem to disrupt the vicious circle of cartilage destruction¹⁵. Prognosis is mostly dependent of the time passed since the onset of infection, further of number of joints involved and the extent of bony lesions. Even in humans, a good outcome can only be achieved with early recognition and immediate and adequate treatment^{16,17}. In case of serous or serofibrinous monarthritis without or with only minor radiological bone changes the prognosis is good. In severe stages of septic arthritis, especially in the tibiotarsal- and stifle joint, prognosis is guarded even with surgical therapy because of the many joint pouches and the complex composition of these joints⁵.

Conclusion

To answer the question asked in the title, synovial structures should be treated if infection has been recognized early. In delayed cases where cartilage or bone is affected, the outcome is usually guarded even when modern drugs and techniques are used. In these cases, treatment depends on the abilities and facilities of the veterinary surgeon(s) and the will of the owner to invest money despite the risk to lose both – money and animal.

Infection of synovial bursae

Inflammation of the calcanea subtendinea bursa: The calcanea subtendinea bursa is situated directly over the *tuber calcanei*, between the gastrocnemius muscle and the superficial flexor tendon. Unilateral disease occurs after blunt or penetrating injury, and bilateral disease is associated with decubital ulcers. Open injuries typically have excessive granulation tissue. Diagnosis is based on location, palpation and ultrasonography, and in certain cases probing of the wound is required. Septic bursitis requires surgical incision of the bursa lateral to the Achilles tendon to allow removal of pus and fibrin and curettage of the *tuber calcanei* if necessary. Postoperative rest and application of a splint or cast are also required. The prognosis for recent injuries is good, whereas chronic injuries with osteomyelitis and tendinitis have a poor prognosis. A subcutaneous false bursa on the tarsus sometimes occurs in older cattle.¹⁸

Inflammation of the „carpal joint extensors“: This refers to inflammation of structures on the dorsal aspect of the carpus and involves the bursa, tendon sheath, tendons and muscles (*extensor carpi radialis*, *extensor digitalis communis*, *abductor pollicis longus* muscles). The precarpal bursa is also frequently involved. Sometimes the bursa of the *extensor carpi ulnaris* muscle communicates with the antebrachio-carpal joint^{19,20} or indirectly with other joints.²¹ This condition is typically very painful with marked hardening of the *extensor carpi radialis* muscle, usually bilaterally. The cause is not known. Young postpartum cows particularly are affected when they are placed in a tie stall shortly before calving. The cows remain standing for hours or even days because it is too painful to lie down and get up again. In sternal recumbency, the limb is extended forward, and sometimes the cows rest in lateral recumbency. Treatment may be attempted with provision of soft bedding, topical preparations, protective bandages, antibiotics and antiinflammatory drugs.¹⁸ The prognosis is guarded in acute unilateral disease and poor to grave in chronic bilateral disease.

Infraspinatus bursa: In adult cattle, the subtendinous bursa of the *infraspinatus* muscle is approximately 6-8 centimeters in diameter and has a thin wall. It starts at the transition between the tendon and muscle and covers the lateral aspect of the major tubercle of the humerus at the insertion of the tendon.²² Inflammation occurs as a result of falls, repeated strains and blunt or penetrating trauma. The affected limb is held in an abducted position to relieve pressure on the inflamed bursa. Ultrasonography is useful for visualization of the enlarged bursa. The size of the bursa and examination of its content allows a definitive diagnosis. Radiography of the shoulder joint, however, is not helpful in visualizing and diagnosing the lesions.²³ The bursa can be easily accessed and incised cranial to the tendon of the *infraspinatus* muscle, after incision of the skin and cutaneous muscle. General or regional infiltration anesthesia can be used. In the acute stages of disease, treatment by lavage of the bursa via a catheter may be a good option. Fibrinous infections (Fig. 1 and Fig. 2) require surgical intervention and curettage. The prognosis is good to favorable, but in patients with purulent infection and lesions of the humeral head, the prognosis is guarded to poor.

Bicipitalis femoris bursa: The bursa is situated between the insertion of the tendon of the *glutaeobiceps* muscle and the lateral condyle of the femur. There is usually bilateral swelling, and cattle have difficulty rising but appear to have no gait abnormalities. Laboratory analyses are unremarkable. The majority of cattle slowly improve with access to pasture or deep straw bedding. The disease worsens in a few, necessitating euthanasia. Necropsy reveals that the stifle swelling consists of connective tissue and necrotic muscle with edema and changes in the bursal fluid. In protracted cases, there may be multifocal connective tissue metaplasia of the bone or osteonecrosis of the tibia. Histologically, there is massive formation of connective tissue with round cells and eosinophils distributed throughout tendons and ligaments.²⁴ In some areas, *onchozercia filariae* are seen in deeper layers. The same filaria are also seen in healthy animals; however, histological lesions in affected animals are much more severe. Surgical treatment is not recommended.

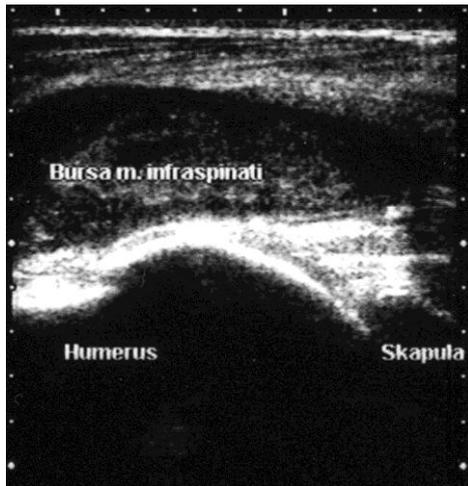


Figure 1: Ultrasonography of the fraspinatus bursa with enlargement and hyperechoic content

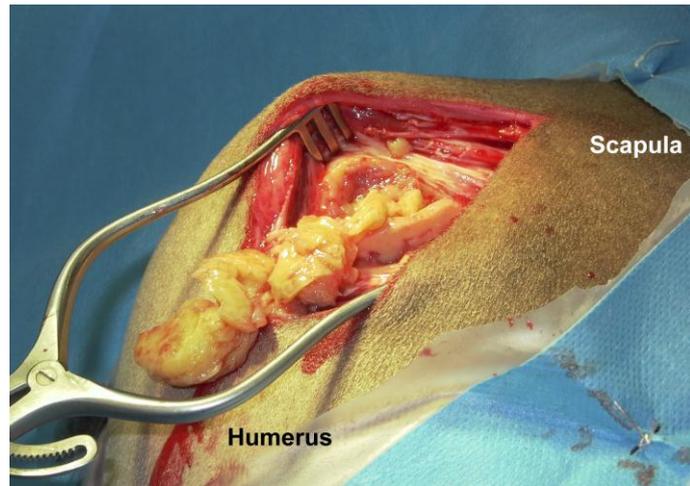


Figure 2: Infection of the left infraspinatus bursa in-relevant region during surgery

Infections of tendon sheaths

Tenosynovitis of the common digital extensor muscles: The common digital extensor muscle is strong and consists of two trunks, each of which has its own tendinous insertion.²⁵ The tendons run together in a common sheath dorsolaterally over the carpus towards the digits. Affected animals show a swinging-leg lameness of the forelimb and do not flex the carpal joint. The region of the lateral aspect of the forearm is swollen and palpation elicits pain. On ultrasonographic examination,²⁶ tissue thickness is increased and anechogenic fluid containing echogenic material can be seen within the tendon sheath. Tenosynoviotomy can be done under general anesthesia but may also be carried out in the field by sedating the cow and using regional intravenous limb anesthesia after placing a tourniquet proximal to the elbow. A straight incision is made over the tendon sheath, which extends to the mid forearm. The tendon sheath is thoroughly lavaged and drains are placed. The tendon sheath is left open and the subcutaneous tissue and the skin are closed, but drainage must be provided. A bandage that includes both claws and a splint are applied for two weeks.

Isolated infection of the tendon sheath of the *lateral digital extensor* muscle has a good prognosis after appropriate surgical treatment (Kofler and Martinek 2004).

Tenosynovitis of the deep flexor tendon sheath at the tarsus: This flexor tendon sheath lies at the medial aspect of the tarsus and extends from about 5cm proximal to the level of the calcanean tuberosity to the level of the tarsometatarsal joint. A communication between the tarsocrural joint and the tendon sheath occurs in approximately 25 % of cattle.²⁷ Treatment of septic tenosynovitis of the tarsal flexor tendon sheath consists of conventional methods (lavage, tenosynoviotomy). With purulent inflammation of the tendon sheath, resection of the tendons may be indicated.²⁷⁻²⁹ In cases with concurrent tarsitis the prognosis depends on the stage of joint infection, but usually is not good.

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