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Equine osteoarthritis: A review of pathogenesis, diagnosis and treatment

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Summary

A brief review of pathogenesis, diagnosis and treatment of equine osteoarthritis is presented.
The role of synovitis in promoting articular cartilage degradation is discussed, and attention is drawn to the fact that chondrocytes themselves seem to be the major contributors of cartilage degradative enzymes.
Various methods of recognizing ongoing cartilage degeneration have been described. The use of these methods allow the establishment of an early diagnosis of osteoarthritis, thus improving treatment options and prognosis.
Treatment of osteoarthritis must be initiated in the early stages of the disease before articular cartilage degeneration has progressed to an irreversible level. Special attention is therefore given to the treatment of synovitis and conditions causing synovitis, as this will minimize the cartilage degradative effects of joint inflammation.

keywords: osteoarthritis, horse, degenerative joint disease

Osteoarthritis des Pferdes: Ein Überblick über Pathogenese, Diagnose und Therapie

Der Autor gibt einen Überblick über Pathogenese, Diagnose und Therapie der Osteoarthritis des Pferdes. Diese degenerative Gelenkserkrankung ist gekennzeichnet durch eine fortschreitende Schädigung des Gelenkknorpels, welcher nur in geringem Umfang regenerierfähig ist.
Die Pathogenese der Osteoarthritis ist weitgehend ungeklärt. Es wird angenommen, daß die akute und chronische Synovitis Auslöser der Erkrankung seien, indem sie den Zusammenbruch des Gelenkknorpels initiieren. Weitere potentielle Ursachen sind direkte Traumen, welche ständig auf das betroffenen Gelenk einwirken, aber auch Chip-Frakturen. Die Entzündung der Synovialmembran scheint deshalb von großer Bedeutung zu sein, da hierbei einige Mediatoren freigesetzt werden, welche Zellschäden verursachen.
Zu diesen Mediatoren gehören Kinin, Histamin, Komplementfaktoren und Metaboliten des Gerinnungssystems. Sie locken Neutrophile und Mononukleäre Zellen an, welche wiederum lysosomale Enzyme freisetzen, so daß freie Radikale entstehen, welche den Gelenkknorpel enorm schädigen. An diesem Entzündungsprozeß sind auch verschiedene Zytokine, Leukotriene und Prostaglandine beteiligt, außerdem gibt es neutrale Metalloproteinasen, welche die Struktur des Gelenkknorpels schädigen, indem Proteoglykane und Kollagene abgebaut werden. Einige In-vitro-Versuche demonstrierten die Rolle des Interleukin-1 bei der Zerstörung des Gelenkknorpels, und des von Chondrozyten produzierten Stromelysins, einer der neutralen Metalloproteinasen. Die Bedeutung der Substanz P bei der Pathogenese der Osteoarthritis ist noch ungeklärt, es wird jedoch vermutet, daß sie die Zytokin- und Prostaglandinsynthese fördert.
Neben der Synovitis wird das rezidivierende Gelenktrauma als Auslöser der degenerativen Osteoarthritis diskutiert. Bei immer wiederkehrenden Traumen kommt es zum Anstieg der Arachidonsäurekonzentration in der Chondrozytenmembran sowie zu mechanischen Schäden am Gelenkknorpel.
Niebauer u.a. beschäftigten sich mit dem Einfluß der immunologischen Reaktivität auf degenerative Gelenksleiden. Sie isolierten Anti-Kollagen-Typ1-Antikörper und komplementgebundene Immunkomplexe aus der Synovialflüssigkeit von Pferden mit Chip-Frakturen oder Osteochondrosis dissecans.
Vermutlich kommt der Synovitis die Hauptrolle bei der Pathogenese der Osteoarthritis zu, daneben erscheint der Chondrozyt selbst die Hauptquelle Knorpel-degenerierender Enzyme zu sein.
Die Diagnose der denegerative Osteoarthritis hängt vom klinischen Erscheinunsbild des Falles ab. Neben Lahmheit, Schwellung des Gelenks und Beugeschmerz fällt oft eine eingeschränkte Beweglichkeit des betroffenen Gelenks auf. Leitungsanästhesien und intrasynoviale Anästhesien helfen, den Sitz der Erkrankung zu lokalisieren. Die radiologisch erkennbaren Veränderungen sind typisch und beinhalten marginale Osteophytenformation, subchondrale Knochensklerose, periosteale Proliferationen, Auflösung des subchondralen Knochens sowie eine Einengung des Gelenkspalts.
Ein wichtiges diagnostisches Hilfsmittel bei der Früherkennung der equinen Osteoarthritis ist die Thermographie, welche bereits geringgradige Entzündungen sichtbar macht. Speziellere Diagnosen werden durch die Szintigraphie erbracht, besonders dann, wenn andere Techniken keine genaue Lokalisation der Erkrankung erbringen. Wenn auf dem Röntgenbild noch keine Veränderungen sichtbar sind, kann eine Arthroskopie des betroffenen Gelenks bereits frühe Schäden wie z.B. Fibrillation und Erosion des Gelenkknorpels aufdecken. Die ultrasonographische Messung der Dicke des Gelenkknorpels liefert ebenfalls Hinweise auf degenerative Prozesse.
Als biochemische Marker der Osteoarthritis gelten die LDH-Isoenzymaktiviät in der Synovia, Glykosaminoglykane und die verschiedenen Produkte der Kollagensynthese. Eine Untersuchung der Synovialflüssigkeit auf Farbe, Konsistenz, Präzipitate und Proteingehalt gibt Hinweis auf eine Synovitis.
Die Behandlung der equinen Osteoarthritis sollte sich auf die Unterbindung der primären Ursachen stützen, da eine Wiederherstellung des Gelenkknorpels kaum möglich ist. Zu den zahlreichen Behandlungsmethoden gehören : Ruhe, kontrollierte Arbeit, physikalische Therapie, intraartikuläre Injektionen von Kortikosteroiden, Hyaluronsäure, Orgotein und polysulphatierten Glykosaminoglykanen, orale oder parenterale Verabreichung von nichtsteroidalen Antiphlogistika sowie chirurgische Eingriffe in Form einer Kürettage, einer Arthrodese oder Fenestration des Gelenks. Es wurde auch versucht, Knorpelschäden durch autogene periostale und osteochondrale Transplantate aufzufüllen, die Resultate waren jedoch sehr variabel. Erste Erfolge wurden durch den Versuch einer Transplantation von Chondrozyten in einer Fibrin-Matrix erzielt.

Schlüsselwörter: Osteoarthritis, Arthrosis deformans, Pathogenese, Diagnose, Pferd

Introduction

Lameness due to joint disease is an important cause of reduced performance in the athletic horse (*Rossdale* et al. 1985), and the economic impact on the racing industry is considerable (*Jeffcott* et al. 1982). Osteoarthritis (OA), or degenerative joint disease (DJD), is a chronic disorder characterized by progressive articular cartilage degeneration, and considering the limited potential of this tissue for regeneration, preventive measures, early diagnosis and treatment are of paramount importance (*Pool* and *Meagher* 1990).

Recognition of the mediators and products of inflammation as important factors in the initiation of articular cartilage degeneration has put an emphasis on the inflammatory response in the pathogenesis of equine OA (*Palmer* and *Bertone* 1994). Acute as well as chronic low-grade synovitis are believed to have the potential for initiating progressive cartilage breakdown, and therefore, adequate treatment of these conditions is essential in the prevention of OA (*Todhunter* and *Lust* 1990).

Recent progress has been made in the development of methods that may be valuable in establishing early diagnosis of equine OA. These methods include various markers of cartilage degradation (*Rørvik* and *Grøndahl* 1995) as well as non-invasive and invasive imaging techniques.

The purpose of this paper is to present a review of the pathogenesis, diagnosis and treatment of equine OA.

Pathogenesis

The pathogenesis of equine OA is still poorly understood, but advances have been made in the clarification of the sequence of events leading to the process of articular cartilage degeneration. Direct trauma as well as the influence on the articular cartilage by synovial membrane inflammation (synovitis) are believed to be important pathways for cartilage degeneration (*McIlwraith* 1982, 1987a; *Clyne* 1987; *McIlwraith* and *Vachon* 1988; *Pool* and *Meagher* 1990).

This is especially true in high-motion joints such as the carpal and fetlock joints (*McIlwraith* 1982, 1987a). In low-motion joints such as the distal intertarsal joints and the proximal interphalangeal joint, repetitive direct trauma to the cartilage could be the main etiologic factor (*McIlwraith* 1982, 1987a; *McIlwraith* and *Vachon* 1988).

The relationship between synovitis and articular cartilage degeneration is complex and not fully elucidated (*Todhunter* and *Lust* 1990; *Palmer* and *Bertone* 1994). Articular cartilage is an avascular tissue and therefore incapable of hosting an inflammatory response, and it is the reaction of this tissue to synovial membrane inflammation that will be discussed below.

Synovitis, of traumatic or septic origin, results in the release of several mediators of inflammation into the synovial fluid (*Todhunter* and *Lust* 1990; *Palmer* and *Bertone* 1994). These mediators include kinin, histamine, complement factors and byproducts of the clotting and fibrinolytic systems. Neutrophils and mononuclear cells are attracted, infiltrate the synovial membrane as well as the synovial fluid, and these cells release lysosomal enzymes and oxygen-derived free radicals (ODFR). Lysosomal enzymes and ODFR are apparently able to degrade cartilage components directly (*Auer* 1989; *Palmer* and *Bertone* 1994). Additionally stimulation of synoviocytes, chondrocytes and macrophages results in the synthesis of various cytokines and metabolites of arachidonic acid (prostaglandins and leukotrienes), thus exacerbating the inflammatory response. Cytokines such as interleukin-1 (IL-1) and tumor necrosis factor (TNF) activate chondrocytic enzyme synthesis and release, and these chondrocyte-derived enzymes include stromelysin, collagenase and gelatinase, collectively known as neutral metalloproteinases (*Caron* 1992; *Price* et al. 1992; *Palmer* and *Bertone* 1994). Neutral metalloproteinases are cartilage matrix degradative enzymes; stromelysin acts by degrading proteoglycan while collagenase and gelatinase degrade collagen. The focus is therefore on the chondrocyte itself as the main mediator of cartilage degradation (*Caron* 1992; *May* et al. 1992a; *Price* et al. 1992).

IL-1 has been isolated from synovial fluid in horses with naturally occurring OA (*Morris* et al. 1990). This finding has been supported by others (*Alwan* et al. 1991a). The effect of IL-1 on equine cartilage has been investigated, using in vitro techniques (*May* et al. 1992b; *Morris* and *Treadwell* 1994), and these studies showed an increase in the production of chondrocyte-derived stromelysin. Further to this, it has been proposed that naturally occurring inhibitors of IL-1 in the synovial fluid may play an important role in controlling IL-1 activity in the joint, thereby influencing cartilage response to increased production of IL-1 (*May* et al. 1992c).

Articular cartilage contains naturally occurring inhibitors of metalloproteinases (TIMPs), and under normal circumstances, the TIMPs and metalloproteinases are believed to control proteoglycan and collagen turnover in the cartilage matrix (*Palmer* and *Bertone* 1994). Synovitis disturbs this balance by stimulating the chondrocytes to further synthesis of metalloproteinases, thus enhancing cartilage degradation.

Apart from chondrocytes, synoviocytes and infiltrating leukocytes also are sources of cartilage degradative enzymes, but substantial inactivation of these enzymes occurs by inhibitors in the synovial fluid such as a_2-macroglobulin (*Caron* 1992).

The role of the neurotransmitter substance P in the pathogenesis of equine OA has recently been discussed (*Caron* et al. 1992). In this study, it was shown that substance P concentrations were significantly elevated in the synovial fluid of osteoarthritic middle carpal joints, compared with normal middle carpal joints in horses. The mechanism by which substance P acts in the pathogenesis of equine OA is unknown, but it has been suggested that it may induce increased synthesis of cytokines and prostaglandins (*Caron* et al. 1992).

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pathway, it has been shown that repetitive trauma to cartilage enhances arachidonic acid concentration in chondrocyte membranes, thereby indicating some direct influence of mechanical impact on chondrocyte metabolism (*Chrisman* et al. 1981). Trauma may also damage the articular cartilage in a more direct physical manner (*McIlwraith* 1982).

It has been suggested that immunologic reactivity might be involved in the mechanisms of chronic inflammation and progressive cartilage degradation in equine OA (*Niebauer* et al. 1988). These authors isolated anticollagen type-I antibodies and complement-binding immune complexes from synovial fluid samples of horses affected with secondary OA as a sequel to chip fractures or osteochondritis dissecans. Type I is the primary collagen of bone tissue and is not a constituent of equine articular cartilage, in which type II is the primary collagen (*Vachon* et al. 1990; *Palmer* and *Bertone* 1994). Anticollagen type-I antibodies are therefore indicative of exposure of bone tissue to the joint cavity. In the study by *Niebauer* et al. (1988), only a few horses had anticollagen type-II antibodies, a finding that was attributed to the presumption that joints are exposed under normal circumstances to small amounts of cartilage debris. Exposure of subchondral bone takes place only in cases of severe trauma, such as chip fractures. The role of immunologic reactivity in equine OA other than secondary OA as a sequel to chip fractures or osteochondritis dissecans is uncertain.

Oxygen-derived free radicals (ODFR) are powerful tissue-damaging inflammatory products whose generation in the joint has been considered important in the pathogenesis of equine OA (*Auer* 1989). These inflammatory products are characterized by their ability to damage tissue directly (*Van-Steenhouse* 1987), and it has been proposed that they may initiate articular cartilage degradation (*Auer* 1989). ODFR are derived either from activated neutrophil leukocytes or from an ischemia-reperfusion cycle. The latter pathway seems to be the most important in the pathogenesis of equine exercise-induced OA (*Auer* 1989). The same author suggests that fluctuations in the synovial fluid oxygen tension during exercise may generate continuous ischemia-reperfusion cycles, thereby generating ODFR in the joint. These ODFR then react directly with cartilage components, thus initiating articular cartilage degradation. In addition, ODFR are believed to influence the activity of cyclo-oxygenase, the enzyme controlling prostaglandin synthesis (*Cleland* 1984), and this interaction could be important to the inflammatory response. In short, ischemia-reperfusion injuries can be explained as follows: Ischemia results in local hypoxia which leads to a reduction of mitochondrial oxidative phosphorylation. As a consequence of this, the concentration of cellular AMP increases, and AMP is subsequently metabolized to hypoxanthine and xanthine. In addition, hypoxia results in increased levels of cellular xanthine oxidase. Reperfusion causes oxygen tension to increase, and hypoxanthine and xanthine oxidase reduce molecular oxygen to the superoxide radical. This radical is then part of the process leading to the formation of the highly reactive hydroxyl radical. The exact role of ODFR in the pathogenesis of equine OA is at the present time not fully elucidated and warrants further investigations.

In summary, synovial membrane inflammation (synovitis) seems to play a major role in initiation and development of cartilage degeneration, the hallmark of equine OA. The primary source of cartilage degradative enzymes is believed to be the chondrocyte itself.

Diagnosis

In a clinical setting, the manifestations of equine OA will vary with the stage of the condition and the degree of joint inflammation (*McIlwraith* 1982, 1987a). Dependent on these factors, the clinical signs may include varying degrees of lameness, heat, swelling, pain on flexion, and decreased range of joint motion. Confirmation that the lameness is referable to a given joint is often obtained by nerve blocks or intrasynovial analgesia. Once the problem is localized, it is customary to perform a radiographic examination of the joints involved.

The radiographic signs of equine OA are generally acknowledged and well documented (*O'Brien* et al. 1971; *McIlwraith* 1982, 1987a). They include marginal osteophyte formation, subchondral bone sclerosis, adjacent periosteal proliferation, and narrowing or loss of joint space. Subchondral bone lysis is a unique feature of OA in low-motion joints (*Pool* and *Meagher* 1990).

It is generally accepted that marked articular cartilage degeneration can be present despite normal radiographic appearance of the joint. It is this fact, that has prompted the search for other diagnostic techniques.

Thermography is a non-invasive method which measures infrared emission from the body, and this technique has a high sensitivity as to detection of low-grade inflammation (*Purohit* 1980; *Purohit* and *McCoy* 1980). Although the technique has limited specificity, it has been suggested as a reliable method for early diagnosis of equine OA (*Vaden* et al. 1980). Thermography can demonstrate vascular changes due to joint inflammation, but no specific information on cartilage degeneration is obtained by this technique. The method should therefore only be used as an adjunct to more specific diagnostic techniques.

Nuclear scintigraphy is a non-invasive imaging technique which consists of injecting a radiopharmaceutical intravenously and using a gamma camera to detect and depict emitted radiation from the body (*Barbee* and *Allen* 1990). The method has primarily been used for diagnosing cases of lameness when other diagnostic techniques have failed to localize the problem (*Devous* and *Twardock* 1984; *Lamb* and *Koblik* 1988; *Chambers* et al. 1995). "Hot spots" of increased activity such as an inflamed or degenerated joint can be identified by this method. Nuclear scintigraphy is sensitive but lacks specificity as to ongoing cartilage degeneration, and this fact limits its usefulness in diagnosing equine OA.

Arthroscopy is an invasive, imaging technique and allows the direct assessment of the articular cartilage (*McIlwraith*

1990). Degenerative changes in the cartilage can be recognized before radiographic evidence of OA occurs, and the typical candidate for diagnostic arthroscopy has a lameness localized in a given joint with no radiographic signs of pathology. Cartilage fibrillation and erosive changes can be identified using this technique, and arthroscopy has gained widespread use in diagnosing early OA and evaluating the extent and character of degenerative cartilage changes. The major disadvantage of this technique is the need for general anesthesia.

Recently, the use of ultrasonography has been proposed as a noninvasive means to evaluate articular cartilage thickness in the horse (*Jørgensen* 1994). The method has been adapted from human medicine where ultrasonography is an integral part of the diagnostic workup in patients with various joint diseases (*Jonsson* et al. 1992). The applicability of the method is limited to cartilage surfaces which lie directly under the skin such as in the dorsal part of the metacarpo/metatarsophalangeal joint and certain parts of the tarsocrural joint. Preliminary results with this technique indicate that articular cartilage degeneration can be recognized ultrasonographically as a general or local thinning of this tissue. Further work is needed before the clinical usefulness of the technique can be fully assessed.

Various biochemical markers of cartilage degeneration have been employed in human medicine, but only a few of these have been investigated in the horse (*Rørvik* and *Grøndahl* 1995). Lactate dehydrogenase (LDH) isoenzyme activity in the synovial fluid has been suggested as a marker of cartilage degeneration (*Rejnö* 1976; *Thorén-Tolling* et al. 1983), but more recent studies have failed to verify the value of this test (*Gängel* and *Rahn* 1992; *McIlwraith* 1993; *Schwierczena* et al. 1993).

Glycosaminoglycans (GAGs) (keratan sulfate and chondroitin sulfate) are part of the proteoglycan molecule in the articular cartilage matrix. Increased levels of these substances have been found in the synovial fluid of horses with naturally occurring OA (*Alwan* et al. 1990, 1991b; *Little* et al. 1990). This fact indicates that GAGs can be used as markers of cartilage breakdown in horses, a presumption which has been supported by experimental data (*Todhunter* et al. 1993a).

Increased collagen synthesis in the articular cartilage of an osteoarthritic joint results in diffusion into the synovial fluid of aminoterminal and C-terminal propeptides. These propeptides are generated when procollagen is converted to collagen. In humans, type II collagen C-terminal propeptide has been suggested as a marker of increased cartilage turnover in osteoarthritic joints (*Shinmei* et al. 1991). Similarly, type III collagen aminoterminal propeptide has been identified as a marker of joint capsule fibrosis in dogs with hip dysplasia and OA in the hip joint (*Madsen* et al. 1990). The author of this publication is part of a team conducting an experimental study of the role of collagen propeptides in horses with OA, and preliminary results indicate that these substances also can be used as markers of joint degeneration in horses.

Further to the role of ODFR in the pathogenesis of equine OA, hydrogen peroxide scavenging ability of synovial fluid has been found to be significantly increased in osteoarthritic compared with normal joints (*Little* et al. 1992). In that study, scavenging ability was significantly associated with the degree of cartilage erosive changes, indicating that the method could be used as a marker of cartilage degradation in equine joint disease.

The presence of cartilage fragments in the synovial fluid has been proposed as a means to identify cartilage breakdown in horses (*Tew* 1982). Not only the presence but also the character of the fragments has been used for identifying cartilage degradation; noncellular fragments were reported to be indicative of superficial cartilage damage, whereas deeper damage supposedly could be evidenced by particles containing chondrocytes and perhaps even subchondral bone tissue (*McIlwraith* 1987b, 1993). This method is now rarely used, because of difficulties in interpreting the results. Other synovial fluid parameters that have been employed when diagnosing equine joint disease include total protein content, relative viscosity, mucinous precipitate quality and white cell count (*McIlwraith* 1987b). Merely being able to indicate the presence of joint inflammation, these methods are unreliable in staging the disease, as to extent of cartilage degradation and should therefore, primarily be used as adjuncts to some of the more specific diagnostic techniques outlined above.

Treatment

The treatment options of equine OA are ruled by the fact that articular cartilage has limited potential for regeneration, and accordingly, the greatest importance has been attached to treatment of primary causes such as intra-articular fractures, septic arthritis, osteochondritis dissecans, and traumatic synovitis (*McIlwraith* 1982, 1987a; *McIlwraith* and *Vachon* 1988). Once articular cartilage degeneration has progressed to a certain level, the possibilities of total joint rehabilitation are believed to be limited, and, at this stage, only palliative treatment options realistically exist.

The various treatment methods are discussed briefly below.

Rest, controlled exercise, and physical therapy are generally accepted as important parts of the management of joint inflammation in the horse (*McIlwraith* and *Vachon* 1988; *Palmer* and *Bertone* 1994). However, these treatment modalities are often combined with more specific medical therapies whose action primarily is to limit synovitis and thereby protect the articular cartilage from the deleterious effects of joint inflammation.

Intra-articular administration of corticosteroids has been used widely in the treatment of equine joint disease (*McIlwraith* 1982). These substances exert powerful anti-inflammatory effects through lysosomal stabilization, blockage of phospholipase A_2, and inhibition of leucocyte migration (*Palmer* and *Bertone* 1994), and this effective suppression of the inflammatory response in the joint is the reason why

corticosteroid administration results in a dramatic decrease in joint swelling and pain. However, several studies have shown that intra-articular administration of corticosteroids results in degenerative changes in the articular cartilage (*Chunekamrai* et al. 1989; *Trotter* et al. 1991; *Shoemaker* et al. 1992), and this deleterious effect should be considered when using these drugs for the treatment of OA. Perhaps the best way to overcome long-term side-effects of corticosteroid administration is to ensure stall rest or limited exercise during the first few weeks after treatment. Although the aim of corticosteroid treatment ideally is to reduce joint inflammation and thus prevent progressive cartilage degeneration, these drugs can also be used as palliative medication in the treatment of later stages of OA when cartilage degeneration is already present. The advent of alternative medications has, however, limited the use of corticosteroids in the treatment of equine joint disease.

Systemic administration of non-steroidal anti-inflammatory drugs (NSAIDs) dampens joint inflammation and reduces pain (*Palmer* and *Bertone* 1994). These prostaglandin inhibitors act by blocking the cyclo-oxygenase enzyme of the arachidonic acid pathway, but they have no direct positive effect on articular cartilage degeneration (*McIlwraith* 1987a). Like corticosteroids, their main effect is that of reducing joint inflammation. In the face of already existing cartilage degeneration, these drugs can merely be used as palliative medication. Evidence exists from human medicine that some NSAIDs have a negative effect on cartilage metabolism. Although similar studies have not been performed on horses, this possible side-effect of NSAID administration could be important. These drugs are often used to prevent lameness in horses in training, but the effect on the articular cartilage of such long-term administration is presently unknown.

Intra-articular administration of exogenous high molecular weight hyaluronic acid (HA) has gained widespread use in the treatment of acute synovitis in the horse (*McIlwraith* 1987a; *Howard* and *McIlwraith* 1993). HA is believed to control the diffusion of various solutes via steric hindrance and to be important to certain cell-to-cell and cell-to-matrix interactions via specific membrane receptors (*Palmer* and *Bertone* 1994). In doing so, it reduces the inflammatory response in the joint. In cases of naturally occurring OA as well as in experimental studies, HA has been shown to improve the clinical signs of OA (*Rose* 1979; *Auer* et al. 1980; *Gingerich* et al. 1981). In a recent study using a cartilage explant system, a chondroprotective effect of HA was suggested in that a decrease in IL-1-mediated proteoglycan release from bovine articular cartilage was observed after addition of HA to the culture system (*Morris* et al. 1992). Further to this, it has been demonstrated that HA reduces the cartilage degradative effect of intra-articularly administered corticosteroids (*Lindholm* 1987). Again, HA treatment should be employed before cartilage degeneration becomes a problem, and although improvement of the clinical signs of OA may occur with this drug, no beneficial effect on already existing cartilage degeneration has been observed.

Polysulphated glycosaminoglycan (PSGAG) is composed of repeating units of hexosamine and hexuronic acid, and treatment with this drug is believed to inhibit cartilage matrix degradative enzymes and to stimulate synthesis of cartilage matrix components (*Hamm* and *Wynn Jones* 1988; *Todhunter* and *Lust* 1994). Both intra-articular and intramuscular applications of PSGAG have been used, and dose levels and intervals have been established (*Hamm* and *Wynn Jones* 1988). The usefulness of the drug in ameliorating the clinical signs of equine OA is generally recognized (*Collins* 1989). The chondroprotective effect of PSGAG has been shown in an experimental study (*Yovich* et al. 1987), but in that same study, no stimulation of cartilage matrix synthesis was observed using a cartilage-defect model. In another study, a positive effect of PSGAG treatment on the development of OA in exercised ponies with experimentally created osteochondral defects was reported (*Todhunter* et al. 1993b). In a tissue culture study, PSGAG was shown to increase net collagen and glycosaminoglycan synthesis by normal and arthritic cartilage (*Glade* 1990). In contrast to this, more recent studies have failed to indicate an anabolic effect of PSGAG (*Caron* et al. 1991, 1993). These somewhat conflicting data necessitate further investigations into the role of PSGAG in the treatment of equine OA. Perhaps this drug is more effective in prevention than in treatment of cartilage degeneration (*Palmer* and *Bertone* 1994; *Todhunter* and *Lust* 1994).

Orgotein exerts superoxide dismutase activity and has anti-inflammatory effects (*McIlwraith* and *Vachon* 1988). It scavenges the superoxide radical, thereby inhibiting ODFR-mediated tissue damage. Results from intra-articular application of orgotein in the treatment of traumatic arthritis have been reported (Ahlengard et al. 1978; Rydén et al. 1987), and the reported data suggest that this substance can be used as an effective anti-inflammatory drug in the treatment of acute synovitis. Its value in the management of OA is, however, still uncertain (*McIlwraith* and *Vachon* 1988). Adverse reactions to intra-articular administration of orgotein have been described (*Wagner* et al. 1982), but the significance of these is unclear.

Surgical treatment of equine OA includes joint curettage, extirpation of osteophytes, and, in low-motion joints, arthrodesis and fenestration.

The aim of surgical curettage of cartilage and subchondral bone in an osteoarthritic joint is to promote healing of degenerate articular cartilage by fibrocartilaginous replacement tissue (*Riddle* 1970), but the quality of such tissue has been questioned (*Hurtig* et al. 1988; *McIlwraith* and *Vachon* 1988). Partial thickness chondrectomy down to smooth and solid cartilage has therefore been advocated as this may ensure a better quality of the remaining articular cartilage (*McIlwraith* and *Vachon* 1988). Further to this, it has been shown in another experimental study that no significant changes occurred in articular cartilage opposing partial thickness lesions in equine carpal joints (*Richardson* and *Clark* 1990). Full thickness defects in the articular cartilage (erosive changes) should, on the other hand, be managed by subchondral bone drilling (forage) as this seems to im-

prove the healing of the defects and the quality of the repair tissue (*Vachon* et al. 1986).

Cartilage resurfacing of experimentally induced osteochondral defects in horses by autogenous periosteal (*Sullins* et al. 1985; *Vachon* et al. 1991a, 1991b) or osteochondral grafts (*Stover* et al. 1989; *Sullins* et al. 1989) has been reported. The purpose of periosteal autografts is to improve the healing of cartilage defects by stimulating repair tissue that resembles hyaline cartilage more closely than the fibrocartilaginous tissue that follows simple curettage. It has been demonstrated that periosteum is more chondrogenic than perichondrium when transplanted intra-articularly in horses (*Vachon* et al. 1989), but cartilage resurfacing by periosteal autografts has been disappointing in experimental studies. The rationale for osteochondral grafting is to transplant viable hyaline cartilage and subchondral bone and to maintain the viability of the transplanted tissues, thus reestablishing a continuous articular cartilage surface. Results with osteochondral grafting have been variable, but this method as well as periosteal transplantation certainly opens new prospects to future research.

Cartilage resurfacing by transplantation of chondrocytes embedded in a fibrin matrix was recently reported (*Hendrickson* et al. 1994). In that study, chondrocyte transplantation to experimentally induced osteochondral defects resulted in repair tissue which had a significantly higher proportion of type II collagen, compared with control defects. This finding is a strong indication for the use of chondrocyte transplantation in cartilage resurfacing of equine osteoarthritic joints in the future, but clinical trials are needed before the method can be completely assessed.

Extirpation of osteophytes is seldom performed and should only be attempted if interference with joint motion can be anticipated (*McIlwraith* 1987a; *McIlwraith* and *Vachon* 1988). Surgical arthrodesis has been described as a treatment of OA in low-motion joints, such as the proximal interphalangeal joint and distal intertarsal joints. The rationale for this treatment is that bony fusion of these joints may lead to athletic soundness. Results and different techniques of proximal interphalangeal arthrodesis have been reported (*Schneider* et al. 1978; *Genetzky* et al. 1981; *Martin* et al. 1984; *Steenhaut* et al. 1985; *Caron* et al. 1990). In the distal intertarsal joints, surgical arthrodesis has gained widespread use in the treatment of OA (bone spavin) (*Adams* 1970; *Mackay* and *Liddell* 1972; *Edwards* 1982; *Wyn-Jones* and *May* 1986).

The surgical technique of fenestration was originally adopted from human osteotomy procedures (*Arnoldi* et al. 1971), the aim being a reduction of the juxta-articular bone pressure. Fenestration has since been widely used in the management of bone spavin in Denmark, and results with this technique have been published (*Sønnichsen* and *Svalastoga* 1985; *Jansson* et al. 1995). A major advantage of this technique is the relatively short period of convalescence, compared with that of surgical arthrodesis (*Jansson* et al. 1995).

The above review of the various treatment methods of equine OA has focused on contemporary therapeutic options, and methods of more historic interest such as the application of blisters and firing have not been the scope of this article and will therefore not be discussed in this context.

Conclusion

Although progress is constantly being made, a lot has yet to be learned about pathogenesis, early diagnosis and treatment of equine OA. The ability to make an early diagnosis of ongoing joint degeneration, combined with an understanding of the pathogenic mechanisms of cartilage degradation and how to control them therapeutically, will in the future undoubtedly improve the prognosis of horses suffering from OA.

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