

Large Animal VETERINARY Rounds®

AUGUST/SEPTEMBER 2006
Volume 6, Issue 7

AS PRESENTED IN THE ROUNDS OF THE DEPARTMENT OF LARGE ANIMAL CLINICAL SCIENCES
OF THE WESTERN COLLEGE OF VETERINARY MEDICINE, UNIVERSITY OF SASKATCHEWAN

Therapy for Equine Joint Disease

By John P Caron, DVM, MVetSc, Diplomate ACVS

Lameness remains an important source of reduced performance in many types of horses and is one of the most common causes of osteoarthritis. The principal concern of many of the owners and trainers presenting these horses for veterinary care is a rapid resolution of the lameness. Ideally, in addition to pain reduction, treatment of joint disease should serve to arrest or slow the progression of lesions (disease modification). This issue of *Large Animal Veterinary Rounds* reviews some of the more common medications used for the treatment of joint inflammation in horses from the perspectives of symptomatic relief (reducing lameness) and disease modification.

Nonsteroidal anti-inflammatory drugs (NSAIDs)

NSAIDs are usually defined as agents that inhibit one or more of the reactions involved in the production of prostaglandins and thromboxanes. Prostaglandins (PGs), particularly those of the E series, are associated with synovial inflammation and cartilage damage and, as such, treating affected horses with NSAIDs appears to be a rational approach.

While NSAIDs possess other anti-inflammatory properties, the principal action of most is inhibition of cyclooxygenase (COX), the first in a series of enzymes responsible for the conversion of arachidonic acid to PGs. The COX enzyme exists in 2 forms and joint inflammation is thought to be primarily due to the production of excessive levels of the second form, COX 2. Pain relief from NSAIDs is mainly, but not exclusively, related to COX inhibition. PGs themselves do not produce pain except when present in large quantities; however, PGs and, in particular, PGE₂ sensitize peripheral nerve endings to mechanical stimuli and amplify the chemical activation of pain receptors by other inflammatory mediators (eg, bradykinin and histamine), both acting to lower the pain threshold. Reducing PG levels also appears to modulate pain perception centrally, at the level of spinal receptors distant from the sites of inflammation. Among their other ancillary mechanisms, NSAIDs may contribute to analgesia by inhibiting sensory neurotransmitter synthesis at the spinal level.

At present, phenylbutazone is the least expensive and most popular agent used in horses and its clinical efficacy appears to compare favourably with other NSAIDs (Table 1). Recently, the basic pharmacology of the other choices for use in horses has been reviewed, including flunixin meglumine, meclofenamic acid, naproxen, ketoprofen, and carprofen.¹ There is considerable variation in the pharmacokinetic profiles of NSAIDs among horses and clearance is influenced by a variety of factors, (eg, the dose and the feeding schedule for orally-administered drugs). These factors should be considered when estimating withdrawal times, given that peak plasma concentrations and apparent half-life can be substantially delayed when NSAIDs are given orally to horses with access to hay.

The disease-modifying (and potentially deleterious) effects of NSAIDs have been investigated *in vitro*; however, the clinical relevance of the results is not clear. Certain NSAIDs are known to inhibit anabolic activities in chondrocytes, while others stimulate matrix synthesis. Fears of enhanced rates of cartilage degradation with NSAID use have not been substantiated in a number of clinical and experimental studies. Indeed, certain NSAIDs have been shown to be chondroprotective in some osteoarthritis (OA) models.

Similar to their effects on cartilage matrix synthesis, NSAIDs appear to vary in their ability to inhibit catabolic events in cartilage and cartilage degradation enzyme activity. While many studies



WESTERN COLLEGE OF
VETERINARY MEDICINE



Department of Large Animal
Clinical Sciences
Western College of Veterinary Medicine

David G. Wilson, DVM, Diplomate ACVS (*Editor*)
Charles S. Rhodes, DVM, MSc (*Dean*)
David G. Wilson, DVM, Diplomate ACVS
(*Department Head*)

Ken Armstrong, DVM, Professor Emeritus
Sue Ashburner, DVM
Jeremy Bailey, BVSc, Diplomate ACVS
Spence M. Barber, DVM, Diplomate ACVS
Albert D. Barth, DVM, Diplomate ACT
Frank Bristol, DVM, DACT, Professor Emeritus
Ray Butler, DVM, Professor Emeritus
John Campbell, DVM, DVSc
Claire Card, DVM, DACT
James L. Carmalt, VetMB, MRCVS, MVetSc,
Diplomate ABVP (Equine)
Terry D. Carruthers, DVM, PhD
Bill Cates, DVM, Professor Emeritus
Chris Clark, VetMB, MVetSc, Diplomate ACVIM
Peter B. Fretz, DVM, Diplomate ACVS,
Professor Emeritus
Paul Greenough, DVM, Professor Emeritus
Jerry Haigh, DVM, Diplomate ACZM
John CS Harding, DVM, DVSc
Steven H. Hendrick, DVM, DVSc
Murray D. Jelinski, DVM, MSc
Katharina Lohmann, DVM, Diplomate ACVIM, PhD
Steve Manning, DVM, Diplomate ACT
Fernando J. Marqués, DVM, Diplomate ACVIM
Reuben J. Mapletoft, DVM, PhD
Colin Palmer, DVM, Diplomate ACT
Lyll Petrie, BVMS, PhD
O.M. Radostits, DVM, Diplomate ACVIM,
Professor Emeritus
Fritz J. Schumann, DVM, MVetSc
Joseph M. Stookey, PhD
Hugh G.G. Townsend, DVM, MSc
Cheryl Waldner, DVM, PhD
Murray R. Woodbury, DVM, MSc

Western College of Veterinary Medicine
Department of Large Animal Clinical Sciences

52 Campus Drive
University of Saskatchewan
Saskatoon, Saskatchewan S7N 5B4

The editorial content of *Large Animal Veterinary Rounds* is determined solely by the Department of Large Animal Clinical Sciences, Western College of Veterinary Medicine



The Canadian Veterinary
Medical Association recognizes
the educational value of this
publication and provides
support to the WCVM for
its distribution.

Table 1: NSAIDs used in horses

Generic name	Recommended dose (mg/kg)	Form (s)	Relative price (in US \$)
Phenylbutazone	4.4 twice on day 1, 2.2 BID (4 days), then 2.2 SID (IV, PO)	Dose = 2.2.mg/kg BID	
		Tablets (1 gm)	1.0
		Paste (12 gm)	2.8
		Injectable	6.9
Carprofen	0.7 SID (IV)	Dose = 0.7 mg/kg SID Tablets (100 mg)	4.2
Flunixin meglumine	1.1 daily for 5 days (IV, IM, PO)	Dose = 1.1 mg/kg SID	
		Granules (500 mg envelope)	5.0
		Paste (1500 mg tube)	12.4
		Injectable (50 mg/mL)	6.8
Ketoprofen	2.2 SID (IV)	Dose = 2.2 mg/kg SID Injectable (100 mg/mL)	27.4
Meclofenamic acid	2.2 SID (5-7 days), then 2.2 SID or less (PO)	Dose = 2.2 mg/kg SID Granules	1.6
Naproxen	10 SID for up to 14 days (PO)	Dose = 100 mg/kg SID Tablets (500 mg)	7.1

have focused on the direct inhibition of degradative enzymes, potential benefits of NSAIDs may result from the suppression of other mediators in the process. For example, in one of the few existing studies using equine tissues, phenylbutazone appears to limit the proteoglycan depletion that accompanies *in vitro* culture of articular cartilage, but the effect does not appear to be mediated by enzyme inhibition.² In summary, phenylbutazone remains an economical and effective treatment for OA pain and joint metabolism and does not appear to have marked unfavourable effects.

NSAIDs are widely used in the management of horses with OA. Side effects, although uncommon at therapeutic dosages, include ulceration of the gastrointestinal tract and renal papillary necrosis. In both cases, the lesions are thought to result from reduced blood flow mediated by suppression of PGE₂. Renal toxicity is unlikely in normally hydrated horses. Periodic monitoring of serum protein concentrations is recommended in horses receiving long-term courses of NSAIDs. Ponies seem particularly susceptible to NSAID toxicity. Finally, phenylbutazone overdoses have been associated with right dorsal ulcerative colitis.

Corticosteroids

Among the medications available for the treatment of arthritis, intra-articular administration of corticosteroids has the most potent anti-inflammatory effect. Corticosteroids have been a mainstay in the treatment of joint disease for nearly 50 years. In addition to their well-known, general anti-inflammatory properties, corticosteroids inhibit the synthesis and release of several soluble mediators involved in the development of OA lesions and their symptoms. Similar to NSAIDs, pain relief is due, in a large measure, to inhibition of PG synthesis, specifically reducing the synthesis of phospholipase A2 and COX 2, key enzymes in the arachidonic acid cascade.

Corticosteroids have demonstrated disease-modifying properties. They are potent inhibitors of a number of cytokines implicated in the articular cartilage degeneration of OA. Indeed, it has been observed that they suppress the expression of two of the most important mediators of cartilage degradation, interleukin-1 (IL-1) and tumour necrosis factor (TNF)- α , at very low concentrations. Furthermore, corticosteroids inhibit the synthesis of degradative enzymes, (eg, matrix metalloproteinases [MMPs] and related enzymes).^{3,4} These *in vitro* observations are supported by the results of animal model studies demonstrating the disease-modifying effects of low-dose corticosteroids without marked effects on chondrocyte health.

There is a longstanding controversy surrounding the use of intra-articular corticosteroids because of concerns that overuse of a pain-free joint may result in accelerated cartilage degeneration. This impression has been compounded by a demonstration of negative effects from corticosteroids on chondrocyte metabolism. Despite the changes in cartilage matrix synthesis that may result from exposure to relatively low concentrations of corticosteroids, the changes are largely reversible. Furthermore, the levels required to adversely influence cartilage matrix synthesis exceed those required to inhibit the synthesis of the aforementioned mediators of degradation. Although adverse effects can follow repeated injections of high-dose corticosteroids, the importance of corticosteroid arthropathy as a clinical entity is contentious. Available research indicates that this event is less prevalent than its wide publicity suggests.^{4,5}

The dosages used for a particular joint depend on a number of clinical variables, including the joint volume, the severity of the inflammation, and the number of joints requiring treatment. Currently, many clinicians use lower doses than were previously recommended. This is in response to the recognition of the dose-related deleterious effects of these agents on anabolic processes in cartilage and

Generic name	Trade name (Manufacturer)	Concentration (mg/mL)	Dose* (mg)	Potency relative to hydrocortisone	Duration of action [†]	Recommended maximum total dose (mg) [‡]
Methylprednisolone acetate	DepoMedrol (Upjohn)	40	40-80	5	Long	200
Triamcinolone acetonide	Vetalog (Solvay)	10	5-15	5	Medium	20

* Dose ranges are somewhat arbitrary and vary according to joint injected. Doses at lower end of range are generally recommended, particularly for small volume articulations (e.g. distal intertarsal and tarsometatarsal).

[†] Initial response and duration of clinical effects vary widely. [‡] Empirical maximum total dose.

the realization that favourable clinical results can often be achieved by relatively low doses. For example, symptomatic relief may accompany an intra-articular dose of as little as 10 mg to 40 mg of methylprednisolone acetate (depending on the volume of the joint), compared to previously recommended doses of 120–200 mg (Table 2). Clinicians should be aware of the risk of septic arthritis that accompanies any intra-articular injection and that, in the case of corticosteroids, symptoms typically appear some time after the initial injection because of the potent anti-inflammatory effects of these preparations. In summary, corticosteroid injections can provide dramatic symptomatic relief and, if used judiciously, they clearly do not cause injuries to joint function or health.

Hyaluronan (sodium hyaluronate)

Hyaluronan (HA) is a glycosaminoglycan composed of the disaccharides D-glucuronic acid and N-acetyl-D-glucosamine. This glycosaminoglycan is an important component of articular cartilage; the characteristic viscoelasticity of synovial fluid is due to its rich HA content and HA serves as the principal lubricant of synovial soft tissues. Initially, through a therapeutic concept known as visco-supplementation, HA was used to take advantage of these

physical properties; however, it is now recognized that HA exhibits a spectrum of pharmacological activity that contributes to its effect on symptoms, as well as its support of joint homeostasis.

HA has demonstrated direct analgesic properties that appear to be due, in part, to reductions in the sensitivity of articular nerve endings. Further, HA has anti-inflammatory properties, including physical (filtering/exclusion) and receptor-mediated pharmacological mechanisms (inhibition of inflammatory cells and mediators), both of which contribute to its analgesic effects. The clinical response to administration varies widely, but is dramatic in some equine patients.

The presumed disease-modifying effects of HA have been the subject of numerous studies, yet the precise mechanisms involved are still incompletely understood. It has been recognized for some time that HA binds to a number of cell membrane receptors and the most important is the cluster determinant (CD)44 receptor. Because varied articular cell types bear the CD44 receptor, it is reasonable to conclude that HA is capable of exerting a variety of biologic effects. Perhaps, most importantly, HA is protective against cartilage matrix loss induced by IL-1 and other inflammatory mediators.

Cell/tissue	Effect	Influence of MW (Daltons)*	Comments
Leucocytes	↓ migration, chemotaxis, adhesion ↓ free radical scavenging	>1 × 10 ⁶ superior to <1 × 10 ⁶ >1 × 10 ⁶ superior to <1 × 10 ⁶	
Synovial fibroblasts (B-cells)	↑ synthesis of HA	0.5 × 10 ⁶ optimal	High concentrations of low MW ↓ synthesis as does MW > 3-4 × 10 ⁶
Chondrocytes/ cartilage	↓ PGE ₂ release	2 × 10 ⁶ superior to 0.2-1.0 × 10 ⁶	
	↓ PGE ₂ release	2 × 10 ⁶ superior to 0.5 × 10 ⁶	
	↓ Proteoglycan release	0.3 × 10 ⁶ = 2 × 10 ⁶	
	↑ PG synthesis	0.8 × 10 ⁶ superior to <0.3 × 10 ⁶	Low MW inhibits synthesis
	↓ IL-1 induced ↓ PG and collagen synthesis	1 × 10 ⁶ superior to <0.5 × 10 ⁶	
	↓ Chondrocyte apoptosis	0.5-0.7 × 10 ⁶ superior to <0.1 × 10 ⁶	1 × 10 ⁶ less effective than 0.5-0.7 × 10 ⁶
	↑ TIMP-1 release	2 × 10 ⁶ superior to 1 × 10 ⁶ superior to 0.5 × 10 ⁶	

HA = hyaluronan; PGE₂ = prostaglandin E₂; PG = proteoglycan; TIMP-1 = tissue inhibitor of matrix metalloproteinases; MW = molecular weight
* Represents general trends in published studies; different results reported for some effects depending on species, experimental design, and HA concentration

Table 4: Hyaluronans used in horses

Trade name	Manufacturer	Molecular weight* (Daltons)	Concentration	Recommended dose†
Equuron	Solvay Animal Health	1.5-2.0 × 10 ⁶	5 mg/mL	10 mg
Equiflex	Chesapeake Biological	1 × 10 ⁶	5 mg/mL	10 mg
HY-50	Bexco Pharma		17 mg/mL	51 mg
Hyalovet (Hyalovet-20)	Fort Dodge/Vetrepharm	4-7 × 10 ⁵	10 mg/mL	20 mg
Hycoat‡	Neogen	> 1.0 × 10 ⁶	5 mg/mL	30 mg
Hylartin V (Hylartil Vet)	Pharmacia and Upjohn	3.5 × 10 ⁶	10 mg/mL	20 mg
Hyvisc	Vetmedica	2.1 × 10 ⁶	11 mg/mL	20 mg
Legend (Hyonate)	Bayer Corporation	3 × 10 ⁵	10 mg/mL	40 mg (IV)
MAP – 5§	Vetrepharm	7.5 × 10 ⁵	10.3 mg/mL (2 mL) 5 mg/mL (10 mL)	20 mg
Synacid	Schering-Plough	0.15-0.20 × 10 ⁶	10 mg/mL	50 mg

* As stated by manufacturer

† Intra-articular dosages are those recommended for small-medium-sized joints (eg, metacarpophalangeal). Some manufacturers recommend twice the dose for larger joints (eg, tibiotarsal).

‡ Marketed as an ophthalmic preparation, but popular for intra-articular use at this dose.

§ Marketed as a topical preparation for wounds, but used intra-articularly.

It has been suggested that HA preparations with a molecular weight exceeding 1×10^6 D provide superior clinical and chondroprotective effects; however, this claim is controversial. Certainly, many salutary effects observed *in vitro* are molecular weight-dependent, but their biological impact *in vivo* is less clear. While many details of the actions of HA with varied molecular weights in diseased joints have yet to be characterized, from available data, it appears that preparations with a molecular weight in the range of 0.5 to 2.0×10^6 D likely provide optimal results (Table 3). Commonly used HA preparations are summarized in Table 4.

In the horse, HA appears to be more effective in the treatment of incipient joint lesions than in established disease where results are often disappointing. This observation parallels clinical experience in humans; individuals with relatively mild radiographic abnormalities demonstrate a better response to HA treatment than those with more advanced changes. Although cost prohibitive in some circumstances, optimal results in horses may accompany a series of 4 to 5 injections at 7- to 14-day intervals.

Corticosteroids and hyaluronan in combination

A relatively popular and potentially beneficial practice is the co-administration of a low dose of a depocorticosteroid and HA. Therapeutic synergy following the use of this combination has been reported for human OA patients and a similar effect in horses is possible. Many clinicians find the idea of combination therapy appealing because it permits a reduced dose of corticosteroid and takes advantage of the protective effects of HA.

Polysulfated glycosaminoglycan

Polysulfated glycosaminoglycan (PSGAG) is a semi-synthetic preparation from bovine trachea that is comprised principally of chondroitin sulfate, a glycosaminoglycan found in the aggregating proteoglycan of cartilage. PSGAG is purported to have both chondroprotective and anti-inflammatory properties; however, the exact nature and mechanism(s) by which it exerts these effects are unknown. Used in humans since the 1960s, PSGAG administration leads to reductions in the severity of clinical signs in human and equine arthritis patients. Clinical improvement is likely attributable to anti-inflammatory effects, including the inhibition of PGE₂ synthesis and of cytokine release. Early reports suggested that PSGAG stimulates the synthesis of proteoglycans and collagen by chondrocytes, an effect ostensibly contributing to the healing of injured cartilage. Subsequent studies have failed to demonstrate any stimulation of proteoglycan synthesis and it is currently accepted that the stimulation of cartilage repair is not among the central mechanisms of PSGAG action. PSGAG also has anticatabolic effects; it is capable of inhibiting the activity of a number of degradative enzymes known to be present in articular tissues. Various animal arthritis models have provided support for a disease-modifying effect of PSGAG *in vivo* and, in most cases, beneficial effects were primarily attributed to the inhibition of degradative enzymes.

PSGAG can be administered intra-articularly or intramuscularly; however, the elevated risk of infection accompanying intra-articular administration of PSGAG (quantitatively exceeding that of corticosteroids) has

reduced enthusiasm for administration by this route. Despite these risks, intra-articular administration remains standard practice for advocates of PSGAG, primarily due to a perception that it provides greater efficacy. It is recommended that intra-articular PSGAG administration be accompanied by an aminoglycoside (eg, amikacin, 125 mg) as a preventive measure. As for other anti-arthritis preparations, the frequency of PSGAG administration is usually based on the therapeutic response and its duration. There is considerable variability in the symptomatic relief with PSGAG treatment; typically, when a favourable therapeutic response occurs, it is rapid.

Nutraceuticals

Recently, there has been a dramatic increase in the popularity of using nutritional supplements to treat and prevent OA in people and domestic animals. Interestingly, the main components of most of these antiarthritis preparations have been researched and used for this purpose for over 20 years. There are numerous substances found in the diverse array of currently marketed products, however, glucosamine and chondroitin sulfate are the components that have received the most intense study and show the greatest potential benefit in the joints of affected animals. Advocates of these and related compounds suggest that their administration may not only provide symptomatic relief of arthritis pain, but also help to prevent the continued degeneration of articular cartilage, the primary and irreversible problem of arthritic diseases. Unfortunately, to date, there is a lack of incisive studies on the *in vitro* effects of glucosamine and chondroitin sulfate, as well as an absence of appropriately designed and rigorous clinical trials; however, available data suggest beneficial effects.

Glucosamine sulfate is a precursor of the disaccharide subunits of cartilage matrix molecules, the proteoglycans. Laboratory studies indicate that glucosamine sulfate increases proteoglycan synthesis by chondrocytes and may have a number of anti-inflammatory activities. Glucosamine also appears to be effective in reducing the suppressive effects of some cytokines on cartilage proteoglycan synthesis. In equine cartilage, glucosamine has been shown to be protective against proteoglycan loss and, in equine cartilage explants, it inhibits the synthesis/activity of degradative proteinases. Recent experiments demonstrate that glucosamine is capable of reducing the synthesis of MMPs induced by inflammatory mediators through diminishing the expression of the genes coding for these proteins in cartilage cultures. In addition, these effects occur at concentrations of glucosamine approaching those achieved by oral administration.^{7,8}

Chondroitin sulfate consists of chains of sulfated galactosamine and glucuronic acid molecules and is the principal glycosaminoglycan of aggregating proteoglycan (aggrecan). Chondroitin resembles PSGAG in structure and, although substantially less richly sulfated, its mechanisms of action are thought to parallel those of PSGAG. Experiments using chondrocytes in culture have provided evidence of the chondroprotective effects of chondroitin sulfate that include stimulation of proteoglycan synthesis and inhibition of matrix degrading enzymes, particularly when chondroitin is present in a polymerized or long-chain form. Chondroitin sulfate also has protective effects on cartilage proteoglycan loss in animal models of joint inflammation.

Lacking an abundance of objective equine *in vivo* data, the results of treatment with glucosamine and chondroitin sulfate in human arthritis patients are of interest because they may provide information about the symptomatic efficacy of these compounds when administered to horses. There are many clinical trials involving human arthritis patients that have generated encouraging results with the use of chondroitin sulfate and glucosamine, alone or in combination. Unfortunately, many suffer from suboptimal design, lack of appropriate controls, and are complicated by the co-administration of other medications. To date, there has been minimal high-quality clinical research conducted on the effects of these compounds in horses.

In summary, laboratory investigations of glucosamine and chondroitin sulfate suggest that they have the potential to provide significant and favourable effects in protecting cartilage from degradation. Symptomatic relief in advanced cases of OA is less than ideal; it may be that these compounds will be used more for the prevention of OA than for therapy of existing disease. It should be recognized that government bodies such as the Food and Drug Administration (USA) do not regulate the formulation of glucosamine and chondroitin sulfate-containing supplements and, therefore, their purity and content are not always assured. The use of products that provide certified contents from reputable sources is recommended.

Summary

The condition of lameness in horses not only represents an economic loss to the owner, but also extracts a significant emotional toll. Most lameness is due to the manifestations of OA. Current treatment modalities include: NSAIDs, corticosteroid injections, hyaluronic acid, polysulfated glycosaminoglycan, and nutraceuticals. Ongoing research efforts are directed toward a more complete understanding of the mechanisms responsible for and involved in the development of OA.

References

1. Goodrich LR, Nixon AJ. Medical treatment of osteoarthritis in the horse - a review. *Vet J* 2006;171:51-69.
2. Jolly WT, Whittem T, Jolly AC, et al. The dose-related effects of phenylbutazone and a methylprednisolone acetate formulation (Depo-Medrol) on cultured explants of equine carpal articular cartilage. *J Vet Pharmacol Ther* 1995; 18:429-437.
3. Borden P, Heller RA. Transcriptional control of matrix metalloproteinases and the tissue inhibitors of matrix metalloproteinases. *Crit Rev Eukaryot Gene Expr* 1997;7(1-2):159-178.
4. Richardson DW, Dodge GR. Dose-dependent effects of corticosteroids on the expression of matrix related genes in normal and cytokine treated articular chondrocytes. *Inflamm Res* 2003;52(1):39-49.
5. Foland JW, McIlwraith CW, Trotter GW, Powers BE, Lamar CH. Effect of betamethasone and exercise on equine carpal joints with osteochondral fragments. *Vet Surg* 1994; 23(5):369-376.
6. Kawcak CE, Norrind RW, Frisbie DD, Trotter GW, McIlwraith CW. Effects of osteochondral fragmentation and intra-articular triamcinolone acetonide treatment on subchondral bone in the equine carpus. *Equine Vet J* 1998; 30(1):66-71.
7. Neil KM, Orth MW, Coussens PM, Chan PS, Caron JP. Glucosamine and chondroitin sulfate regulation of mediators of osteoarthritis in recombinant equine interleukin-1, stimulated equine chondrocytes in pellet culture. *Am J Vet Res* 2005;66(11):1861-1869.
8. Chan PS, Caron JP, Rosa GLM, Orth MW. Effect of glucosamine and chondroitin sulfate on regulation of gene expression of proteolytic enzymes and their inhibitors in interleukin-1-challenged bovine articular cartilage explants. *Am J Vet Res* 2005; 66(11):1870-1876.

Dr. John Caron is a Professor of Equine Surgery at Michigan State University. He is a former Equine Health Research Fellow at the Western College of Veterinary Medicine, University of Saskatchewan. He has investigated various elements of joint metabolism and the effects of antiarthritis medications on joint tissues since 1989.

Abstract of Interest

Effects of 6 α -methylprednisolone acetate on an equine osteochondral fragment exercise model

FRISBIE DD, KAWCAK CE, BAXTER GM, TROTTER GW, POWERS BE, LASSEN ED, MCILWRAITH CW. FORT COLLINS, COLORADO

OBJECTIVE: To determine effects of intra-articularly administered 6 α -methylprednisolone acetate (MPA) in exercised horses with carpal osteochondral fragmentation.

ANIMALS: 18 horses: 3 groups of 6 each.

PROCEDURE: An osteochondral (chip) fragment was created in 1 randomly chosen middle carpal joint of each horse. Polyionic fluid (PF) was injected into both middle carpal joints of horses in the control group. In horses of the MPA-control group, MPA was injected into the middle carpal joint without an osteochondral fragment; a similar volume of PF was injected into the contralateral middle carpal joint. In the MPA-treated group of horses, 100 mg of MPA was injected into the middle carpal joint containing the osteochondral fragment; a similar volume of PF was injected into the contralateral joint. Injections were administered on post-

surgical days 14 and 28, and horses were exercised on a high-speed treadmill for 8 weeks, starting on postsurgical day 15.

RESULTS: Clinical improvement in degree of lameness was not associated with MPA administration. Joints that contained an osteochondral fragment and were treated with MPA had lower prostaglandin E₂ concentration in synovial fluid, and lower scores for intimal hyperplasia and vascularity in synovial membrane, compared with PF-treated joints. However, articular cartilage erosion and morphologic lesions suggested possible deleterious effect of intra-articular MPA administration.

CONCLUSIONS: Some beneficial effects of MPA administration on synovial fluid and synovial membrane were identified; however, the deleterious findings contrast with those associated with triamcinolone acetonide used in a similar model, but agree with other results of MPA administration in normal and abnormal joints.

Am J Vet Res 1998;59(12):1619-28.

Upcoming Meetings

21 – 23 September 2006

39th Annual Convention of the American Association of Bovine Practitioners

Saint Paul, Minnesota

Contact: www.aabp.org

15 – 19 October 2006

24th World Buiatrics Conference

Nice, France

Contact: Service Gestion des congrès

Tel: 00 33 (0)4 93 92 81 61/58

Fax: 00 33 (0)4 93 92 83 38

E-mail: wbc2006@nice-acropolis.com

Website: www.wbc2006.com

2-6 December 2006

52nd Convention of the American Association of Equine Practitioners (AAEP)

San Antonio, Texas, USA

Contact: E-mail: aaepoffice@aaep.org

Website: www.aaep.org

Dr. Caron has stated that he has no disclosures to announce in association with the contents of this issue.

Change of address notices and requests for subscriptions to *Large Animal Veterinary Rounds* are to be sent by mail to P.O. Box 310, Station H, Montreal, Quebec H3G 2K8 or by fax to (514) 932-5114 or by e-mail to info@snellmedical.com. Please reference *Large Animal Veterinary Rounds* in your correspondence. Undeliverable copies are to be sent to the address above. Publications Post #40032303

This publication is made possible by an educational grant from

Schering-Plough Animal Health

© 2006 Department of Large Animal Clinical Sciences, Western College of Veterinary Medicine, which is solely responsible for the contents. The opinions expressed in this publication do not necessarily reflect those of the publisher or sponsor, but rather are those of the authoring institution based on the available scientific literature. Publisher: SNELL Medical Communication Inc. in cooperation with the Department of Large Animal Clinical Sciences, Western College of Veterinary Medicine. [®]*Large Animal Veterinary Rounds* is a registered trade mark of SNELL Medical Communication Inc. All rights reserved. SNELL Medical Communication Inc. is committed to the development of superior Continuing Medical Education. The administration of any therapies discussed or referred to in *Large Animal Veterinary Rounds* should always be consistent with the recognized prescribing information in Canada.