**Take Home Message:** There are a number of options for the treatment of traumatic joint disease and recommendations have been modified based on new research and clinical evaluation in the field. Treatments that have received scientific validation include aquatic therapies, extracorporeal shock wave therapy, NSAIDs, intraarticular corticosteroids, intraarticular, intravenous and oral hyaluronan (HA), intraarticular polysulfated glycosaminoglycan and intramuscular pentosan polysulfate. There is limited scientific evidence for oral joint supplements.

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I. INTRODUCTION

It has been suggested that 60% of lameness problems are related to osteoarthritis (OA).\(^1\) This stresses the importance of advancements in both medical and surgical treatment options. The goal of treatment in all traumatic joint injuries is to return the joint to normal as quickly as possible and prevent the occurrence or reduce the severity of OA. In other words, we need to reduce pain and minimize progression of joint deterioration. Timely removal of osteochondral fragments, fixation of intraarticular (IA) fractures, accurate diagnosis of ligamentous and meniscal injuries and appropriate treatment of osteochondritis dissecans (OCD) entities are also critical treatments to prevent OA.

Two main properties are recognized with medications for equine traumatic arthritis and OA 1) symptom modifying OA drugs (SMOADs) and 2) disease modifying OA drugs (DMOADs) and this is based on improvement of clinical signs in the first category and proof that progressive OA disease has been modified in the second category. Ideally, we want a treatment that positively affects both symptom modifying and disease modifying effects but the second is critical to long-term joint health. Synovitis is the main target for therapy and is important because of pain and joint effusion as well as the production of various harmful mediators including metalloproteinases (MMPs), aggrecanases, prostaglandin E2, free radicals and cytokines such as interleukin-1 (IL-1) and tumor necrosis factor-alpha (TNF-α).

II. TREATMENT OF SYNOVITIS AND CAPSULITIS (AND LONGER-TERM OA)

The following treatments have various levels of evidence for effectiveness and will be discussed.

**Physical Therapy and Rehabilitation:** Swimming and underwater treadmilling have become popular rehabilitation tools after arthroscopic surgery. The use of aquatic therapies and what is known about them in the horse has been recently reviewed.\(^2\) The author has used underwater treadmilling post-surgery in the majority of cases after arthroscopic surgery. More recently, work in the OA chip fragment model has shown that underwater treadmill exercise can positively affect some outcome parameters with experimentally induced carpal joint OA and also positively affect postural sway as an indicator of improved proprioception.\(^3\)

**Extracorporeal Shockwave Therapy (ESWT):** This is one non-medical and non-surgical physical therapeutic tool that has been studied in a controlled fashion in the horse. Again, in the equine carpal OA model ESWT decreased lameness in synovial fluid parameters of inflammation supporting a pain and inflammation method of action.\(^4\) Experimental design did not address DMOAD effects very well. However, evaluation of the effect of ESWT on subchondral bone revealed no significant changes but there were increases in serum biomarkers indicative of bone remodeling (serum osteocalcin concentration was significantly greater in horses that received ESWT compared with placebo treated horses and serum concentrations of C-terminal telopeptide of type I collagen was significantly higher in horses that received ESWT).\(^5\)

**Nonsteroidal antiinflammatory drugs (NSAIDs):** These are antiinflammatory agents that inhibit some component of the enzyme system that converts arachidonic acid into prostaglandins and thromboxane. The topic has been reviewed previously. It does offer a mechanism of selecting a specific level of intervention (generally inhibiting cyclooxygenase). They remain the standard of care for the first line of treatment.
for traumatically induced inflammation. They are also routine pre- and post-orthopaedic surgery. Phenylbutazone and flunixin meglumine are the most commonly used. More recent developments have been new cyclooxygenase-2 (COX-2) preferential inhibitors and topical application but these should not be viewed as absolute replacements to phenylbutazone and flunixin meglumine.

Controversial aspects with NSAIDs have been potential performance enhancement and the Fédération Équestre Internationale’s (FEI) blanket prohibition on the use of NSAIDs in equine athletes during competition needs to be questioned with regard to welfare of the horse. The World Anti-Doping Agency (WADA) permits the unrestricted use of NSAIDs during competition but a general prohibition of the use at any level by FEI is a challenge.

Phenylbutazone is the most common NSAID used in the horse (based on efficacy, availability and affordability) and can be given orally or intravenously. It is relatively non-toxic at repeated doses of 2.2mg/kg twice daily or less and it has been shown that a single dose of 4.4mg/kg markedly reduced PGE2 and PGF2 production in exudate for up to 24 hours and this is explained by accumulation of PBS in inflammatory exudate leading to an elimination T1/2 in exudate of 24 hours (proteinaceous nature of inflammatory fluid and high degree of protein binding of PBS probably explains this); hence, the recommendation for single daily dosing. There have been a number of studies that have shown significant reduction in lameness with experimentally induced synovitis. The use of NSAIDs in racehorses has been challenged but there is very little evidence of harmful effects or risk to injury. However, the AAEP Racing Medication Taskforce has addressed this as well as the Racing Medication and Testing Consortium (RMTC) and RMTC has recommended lowering the permitted level of PBS from 5µg/mL to 2µg/mL. The British Equine Veterinary Association made a submission on supporting the FEI position with NSAIDs in August 2010 that would be at variance with the author’s recommendations and RMTC policy in the US. There is some evidence to support that high levels of NSAIDs when there is pre-existing pathologic change is a risk factor and it has been shown that mineral apposition rate (MAR) and regional acceleratory phenomenon (RAP) were significantly reduced in horses given high (4mg/kg q 12 h) doses and filling of cortical defects was also greater in the control horses.

Known negative effects include gastric ulceration and effect on renal function and pathology. It has been pointed out that provided drugs are used at clinical dose rates such problems are uncommon. Is phenylbutazone harmful to articular cartilage? – there is contradictory in vitro information. In a human study using MRI users of COX-2 inhibitors had decreased lesion development in the medial compartment of the knee where users of conventional NSAIDs had increased defects in both medial and lateral compartments. In a comparative study between firocoxib and phenylbutazone in horses, the results concluded that improvement was more frequent in the firocoxib group than in the phenylbutazone group in all categories except lameness.

Topically administered diclofenac is available in the horse and examination of diclofenac liposomal cream compared with phenylbutazone and controls in the CSU equine OA model showed both symptom modifying and disease modifying effects in OA joints. Baseline lameness was improved in diclofenac over phenylbutazone horses but PGE2 concentration was reduced more in phenylbutazone treated joints compared to diclofenac joints. On histology, there was significant improvement in staining for proteoglycan content compared to both control and phenylbutazone groups, which indicates a disease modifying effect.

There are two forms of cyclooxygenase: COX-1 and COX-2. The latter is induced with inflammation. Naproxen, carprofen and meloxicam are relatively more effective against COX-2 and they will reduce side effects to inhibition of COX-1. Firocoxib is now available in the US.

Corticosteroids: This topic has been reviewed relatively recently. Intraarticular therapy is used frequently. The untoward effects are generalized and often fictitious and the commonly used ones have been carefully evaluated at 14 days and 35 days with no deleterious side effects on articular cartilage and in addition, exercise was beneficial in the presence of fragmentation. On the other hand, examination of methylprednisolone acetate (MPA) in the OA model showed that while there was antiinflammatory effects there was also articular degeneration based on Modified Mankin scores being significantly increased. It is also to be noted that even if MPA was injected into the joint opposite to where the chip fragment occurred there was still negative effects on the cartilage. The third study with triamcinolone acetonide TA tested with the same experimental design as MPA showed a significant reduction in lameness but no negative effects on the articular cartilage with the Modified Mankin scores being significantly lower with TA being injected in the OA joint or in the opposite joint compared to the controls (chip fragment alone treated with placebo).

There has always been concerns on the potentiation of laminitis with triamcinolone but more recent studies suggest that one can use a 40mg total dose without risk. In a UK legal case there was indeed laminitis associated with 80mg of TA in each tarsus and 20mg of dexamethasone into the back. A review of the literature said there was good evidence lacking for an association between intraarticular corticosteroids and laminitis but a large multicentric trial was needed. A review of 2,000 cases with an upper total body dose of 20-45mg reported 3/2,000 (0.15%) having laminitis.

In a review of current joint therapy usage in equine practice, the majority of the respondents (77%) used TA to treat high motion joints and 73% use MPA to treat low motion joints. Veterinarians treating the Western Performance and sport horses were significantly more likely to use TA in high motion joints compared to MPA (p=0.0201 and p<0.0001, respectively). Triamcinolone acetonide use compared to MPA in high motion joints by racehorse veterinarians was significantly lower compared to other veterinarians (p<0.0001).
There have been anecdotal associations of intraarticular corticosteroid use with catastrophic injury. However, work by Kawcak et al and Murray et al refuted any harmful effects of TA or MPA on subchondral bone. This does not diminish the importance of catastrophic injury and the potentiation of injury if disease is masked.

**Hyaluronan (HA):** The proposed mechanisms of action of HA include soft tissue lubrication, steric exclusion and antiinflammatory effects. Original clinical studies were done in Standardbreds and a randomized, double blind, placebo controlled study in 77 Standardbred horses showed that treatment groups consisting of 20mg of intraarticular HA two times and 250mg of polysulfated glycosaminoglycan (PSGAG) 4 times intraarticularly were both superior to 2mL of saline intraarticularly. More recently, intraarticular HA has been tested in the CSU equine OA model with treatments of 20mg at 14, 21 and 28 days. There was a trend for decrease in synovial membrane vascularity and subintimal fibrosis but significantly less articular cartilage fibrillation with HA, demonstrating that there were DMOAD effects with this drug. Hyaluronan has also been tested intravenously with treatments in the OA model at 13, 20 and 27 days (40mg IV). Efficacy demonstrated at day 72 included significant reduction of PGE2 in protein levels in the synovial fluid, decreased synovial membrane vascularity and synovial membrane cellular infiltration as well as significantly decreased lameness.

Clinical use with IV HA has met mixed reaction but it is commonly used prophylactically. One study in racing Quarter Horses demonstrated that the horses raced better but because they qualified for futurities received more intraarticular injections of corticosteroids. In another study (unpublished) racing Thoroughbreds were treated with three injections and no significant differences were shown in biomarkers.

The use of oral HA has become common in more recent years. In one controlled study where oral HA was given after arthroscopic surgery in tarsocrural OCD, a positive effect was demonstrated. Twenty-seven joints in 24 yearlings were treated with 100mg orally for 30 days post-op whereas another 30 joints (24 yearlings) were treated with placebo orally for 30 days. Synovial effusion was scored by a blinded examiner at 30 days (grade 0-5) and the mean 30 day effusion score in the treated group was 0.67 vs. 2.05 in the placebo group (p<0.001).

**Polysulfated glycosaminoglycan:** There is much literature regarding the use of this drug including basic science and clinical studies in humans. This could be considered the prototype DMOAD and was initially developed in Germany for use in humans. An important issue to note when we discuss PSGAG is that all the positive studies are with IA use. There were three studies done between 1982 and 1984 in models of equine OA that we don’t consider very appropriate. A pivotal controlled study was done with the osteochondral fragment-exercise OA model that reported IA treatment with 250mg of PSGAG at days 14, 21 and 28 and was also compared to IA HA (20mg).

The scientific support for IM use of PSGAG (at least at a dose of 500mg) is quite weak. In an earlier study with 500mg of PSGAG every 4 days for seven treatments in a monoiodoacetate (MIA) model showed slight improvement in safranin O staining as the only positive effect. In a second study using the CSU osteochondral fragment model, where IM PSGAG was used as a positive control group in a study on the effect of extracorporeal shock wave treatment, every 4 days (500mg IM) for 28 days starting at the time of OA induction showed no significant clinical or disease modifying effects compared to the control group (IA saline). It is surmised that this is probably a dose effect but this is the dose that is commonly used in practice and higher doses would hardly be economically feasible.

### III. ACKNOWLEDGMENTS

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