

Protection and Support for Joints

This document reviews:

- How and why injury to horse's joints may occur as a result of normal exercise, training and competition
- Joint structure and function
- The rationale for inclusion of different compounds in "joint supplements"

Background

Musculo-skeletal injuries are the most common cause of injury and lost training time in athletes, whether human, canine or equine. Daily exercise and the rigours of competition inevitably cause some damage to the skeleton. This may be compounded by factors such as hard going. The body has a tremendous capacity for repair and provided the components for repair are available in sufficient amounts, for example, through the diet, under normal circumstances repair keeps pace with damage. However, it is not uncommon for damage to exceed the capacity for repair and for pathological changes to take place in the skeleton, leading ultimately to lameness.

Osteoarthritis

Wear and tear on the skeletal system, particularly the articular cartilage surfaces of joints, could be considered to be an inevitable consequence of exercise or simply getting older. Degenerative joint disease (DJD) sometimes referred to, as osteoarthritis (OA), is seen to increase with age and is generally an indication of 'wear and tear'. OA is not uncommon in human gymnasts and other athletes in their later life. The prevalence is much greater in sports where there is considerable weight bearing exercise, such as weight lifting and sports involving jumping, as this increases the loading on the joints.

Is the horse at high risk from Osteoarthritis?

In proportion to its body weight, the horse has relatively little joint surface across which to support its weight, perhaps 70-80 cm² per joint. There are of course 4-5 joints per leg and four legs. But these joints must support all the body weight between them. However, there are many times during exercise when this is not the case and one limb may be subjected to extreme loading. During the gallop, there is a period when all the weight is supported by one limb. Similarly, when landing from a jump, there is a moment when all the weight will be born by one limb.

*It should not be surprising that horses suffer so many musculoskeletal injuries, it should be a surprise that they do not suffer **more!!***

Part of the reason why domesticated horses experience so many injuries related to the skeleton may be due to the fact that they did not evolve to do what we have found we can do with them. In the wild the horse spends 95% of its time grazing, with the rest of

its time taken up by sleeping, playing and grooming. The time budget of a wild horse does not include daily intense exercise (galloping), repeated jumping or prolonged low intensity exercise. However, these are all components of the training programmes for racehorses, showjumpers and eventers and endurance horses, respectively. Whilst it has not been studied, it would be highly likely that wild horses do not suffer from OA either as severely or as commonly as their domesticated and trained counterparts.

A horse's joints effectively act as 'shock absorbers' to concussion and must provide a lubrication system to reduce the friction involved in movement between the joint surfaces. It is most often the synovial joints that are affected by injury or disease, as these are the most active joints, with the fetlock, knees and hock joints being the most commonly affected. The risk of developing OA should increase with intensity and or duration of exercise, years in training, time spent on hard ground, the amount of jumping exercise, but conformation can also play a key role in the development of some forms of joint disease. Conformation is commonly determined genetically but changes in conformation may result from farriery and undiagnosed chronic changes in the musculoskeletal system.

Joint Structure and Function

The articular surfaces of the ends of bones within a joint where they meet (oppose) are protected by a layer of slippery cartilage, which when properly lubricated allows for frictionless movement of the joint concerned and also has the ability to absorb the shock being transmitted up the limb from the impact of the foot with the ground. The joint itself is contained within a joint capsule, which attaches to both bones and is stabilised by ligaments. An essential component of normal joint function and health is continued lubrication of the joint, which reduces the damaging effects of friction. If the fluid is removed the joint will begin to grind itself away, in the same way, as a car engine without oil will quickly seize up.

Synovial Fluid

The synovial membrane lines the joint capsule and secretes a lubricating substance called synovial fluid, which is composed of a number of ingredients including **hyaluronic acid** and **lubrican**.

Cartilage

Cartilage is composed of specialised cells called chondrocytes, which synthesise and deposit a water-based matrix containing collagen and large molecules known as **proteoglycans**. Proteoglycans consist of a **protein core** with side chains of **glycosaminoglycans** (predominantly **chondroitin sulphate**). Proteoglycans are also found in association with **hyaluronic acid**. The arrangement of these components is similar to that of a fir tree, with hyaluronic acid representing the branches, protein the twigs and the proteoglycans (chondroitin sulphate) the needles. The presence of collagen in the cartilage matrix gives cartilage its strength, whilst the proteoglycan in association with hyaluronic acid provides both resilience and flexibility.

Chondrocytes have the ability to synthesise all the components of the cartilage matrix, which is constantly changing. Throughout life the cartilage matrix is slowly removed or replaced in a continuous turnover process. The balance between the synthesis and degradation of cartilage is central to continuing joint health and a failure to maintain this balance is one of the crucial early processes in degenerative joint disease. The disruption to the structure and function of cartilage during degenerative joint disease is thought to arise from an inability of the chondrocytes synthetic capacity to keep pace with the matrix damage caused by **inflammatory mediators** and **degradative enzymes**. The rate of cartilage turnover is very rapid in a foal and gradually declines with age. The turnover rates of the proteoglycan component of cartilage is much more rapid than that of collagen. However, once cartilage has been destroyed it cannot be replaced.

Cartilage is unusual in that it does not have a **blood or nerve supply** and obtains its nutrients from the synovial fluid *via* the lymphatic system. As a result, the supply of nutrients to cartilage is dependent on the volume of synovial fluid. It has been suggested that even in a healthy joint, the volume of synovial fluid is on the limit of that required to sustain normal cartilage turnover. Any increase in the stresses imposed on joints through training or competition, especially on hard ground, or an increase in the degradative process as a result of injury or cumulative wear and tear will increase the requirement for those components of the diet needed to maintain the cartilage's structure and integrity.

Dietary “Joint Supplements”

Recently there has been a dramatic increase in the number of supplement products on the market that contain a variety of nutrients promoted as being beneficial to joint cartilage health and regeneration. There has been a parallel increase in the amount of scientific evidence both in humans and horses to support a role for nutrition in conditions such as degenerative joint disease/osteoarthritis. These nutrients are globally referred to as **chondroprotective** and have one or more of the following attributes.

- Reduce inflammation of the synovial membrane (synovitis).
- Increase the synthesis of hyaluronic acid by other specialist cells called synoviocytes, which will improve lubrication but may also improve the delivery of nutrients.
- Stimulate chondrocytes to produce cartilage matrix compounds.
- Reduce joint pain (anti-inflammatory action).
- Inhibit cartilage-degrading enzymes.

Some of the commonly seen ingredients in 'joint supplements' exhibit one or more of these properties.

❖ **Chondroitin Sulphate (CS)**

Chondroitin Sulphate is a component of the naturally occurring proteoglycans in the body and is formed from repeating units of ***N-acetyl glucosamine*** and ***glucuronic acid***. Chondroitin sulphate or its components are common ingredients in joint supplements and its precise structure is dependant on where it is sourced. In mammalian cartilage the sulphate group in glucosamine is at position 4 (Chondroitin Sulphate A) whilst in fish cartilage the sulphate is at position 6 (Chondroitin Sulphate C). Chondroitin Sulphate for inclusion in supplements is normally extracted from bovine, porcine or marine sources. Chondroitin sulphate from these sources has a molecular weight of 50,000 – 100,000 Da or (50-100 KDa) but following the extraction process this may be reduced to 10,000 – 40,000 Da, dependent on the raw material source and processing.

Functions of Chondroitin Sulphate

- **Anti-inflammatory:** Chondroitin sulphate has anti-inflammatory properties acting *via* phospholipase A2 and prostaglandins.
- **Protection:** Chondroitin sulphate helps protect the cartilage from the action of destructive metalloproteinase enzymes and has also been shown to decrease collagenase activity - the enzyme that destroys collagen.
- **Controls water content of the cartilage matrix:** Chondroitin sulphate attracts water by maintaining and controlling the osmotic pressure within the cartilage, so helping control levels of hydration, thus maintaining flexibility and elasticity.
- **Reducing friction:** Chondroitin sulphate improves synovial fluid viscosity by increasing hyaluronic acid concentration.

Absorption of Chondroitin Sulphate

There has been recent debate as to the degree of chondroprotection offered by chondroitin sulphate. In addition, there has been further debate over its supposed bioavailability. Some studies have demonstrated increases in plasma, urinary and synovial chondroitin sulphate concentrations following oral administration. Conversely other authors have reported little or no chondroitin absorption. The presence of low molecular weight fragments of chondroitin sulphate, including monomer, oligo and polysaccharides fragments, have been found in plasma, tissue and urine following oral dosing. There are no intestinal, pancreatic or brush border enzymes that are capable of

degrading such polymers, however bacterial degradation in the large intestine could be involved.

Studies in rats have shown that the chondroitin sulphate polymer is not degraded in the stomach or small intestine but is degraded by bacteria resident in caecum, and to a lesser extent in the colon, to low molecular weight metabolites. The degree of degradation appears to be related to the residence time in either the caecum or colon. Studies in rats with radiolabelled chondroitin sulphate suggest that a small proportion of the chondroitin sulphate is absorbed intact in the small intestine and colon, whilst the majority is degraded in the caecum and absorbed as small molecular weight fragments. These studies also reported that there was no difference in the rate of degradation of chondroitin sulphate according to molecular weight between (molecular weight 10 – 18,000kDa).

Key Points

- Chondroitin sulphate appears to be absorbed intact to a small extent in the small intestine and colon but is rapidly degraded to small molecular weight metabolites in the caecum.
- Despite this, there are numerous scientific studies confirming the efficacy of chondroitin sulphate for osteoarthritic disease and so its chondroprotective effects should not be discounted.
- Recent work in horses suggests that chondroitin and glucosamine are effective synergistically *in vitro*.

❖ Glucosamine

Glucosamine is normally **synthesised from glucose** and forms part of the structure of the glycosaminoglycan chains within the structure of proteoglycans. It is isolated from the hydrolysis of **crustacean shells** to form the hydrochloride or sulphate salt.

Functions of Glucosamine

- **Collagen synthesis:** Stimulates the manufacture of collagen.
- **GAG stimulation:** Glucosamine stimulates cartilage chondrocytes to produce GAG's.
- **Decreases nitric oxide production:** Nitric oxide is one of the factors involved in cartilage degradation.
- **Reduced formation of prostaglandin E2:** a potent inflammatory mediator.

- **Inhibits matrix metalloproteinase enzyme activity:** involved in cartilage degradation.

Absorption of Glucosamine

Glucosamine has been shown to be rapidly absorbed and concentrates in articular cartilage. It is a small molecule that is soluble in water and bioavailability is reported as being high in all species studied. It has been shown to be the preferred substrate for synthesis of glycosaminoglycans and its availability is likely to be a rate-limiting step for their synthesis.

Combined use of Glucosamine and Chondroitin Sulphate

There is evidence to support the use of both glucosamine and chondroitin sulphate to slow the degeneration of cartilage tissue, and there is therefore logic to provide the two together in order to benefit from any synergistic effects as the two substances act in slightly different ways. There is some *in vitro* work to suggest that there may be a complementary effect of glucosamine and chondroitin sulphate on the maintenance of joint function. However, there is no direct evidence as yet to support that a combined product is more efficacious than either of the two components alone.

Key Points

- Glucosamine is normally synthesised from glucose and forms part of the structure of the glycosaminoglycan chains within the structure of proteoglycans.
- Glucosamine has been shown to be rapidly absorbed and concentrates in articular cartilage.
- The beneficial effect of glucosamine on the maintenance of joint function in horses, dog and man has been published in scientific journals

❖ MSM

MSM or methyl sulphonyl methane is a naturally occurring compound found in both plants and animals that supplies an **organic and bioavailable form of sulphur**. It occurs naturally in the horse's diet, however drying or processing will destroy the majority. **MSM consists of about 34% sulphur** by weight and together with its related compounds, is the source of over 80% of the sulphur found in all living organisms. MSM is a derivative of **DMSO** (dimethyl sulphoxide), which is routinely used in veterinary medicine for a number of applications, including treatment of musculo-skeletal problems through its **anti-inflammatory and analgesic action**.

Functions of MSM

- **Sulphur Donor:** provides sulphur to repair damaged sulphur-containing bonds such as those found in collagen.
- **Anti-inflammatory:** evidence from both man and horse both *in vitro* and *in vivo*.
- **Analgesic:** some evidence for analgesic action.

MSM is found naturally in the body but the levels are found to decrease with age. The sulphur content of arthritic cartilage has been reported to be only 30% of that found in normal human cartilage. The effects of MSM are thought to be mediated through its action as a sulphur donor to repair damaged sulphur-containing bonds such as those found in collagen. Several studies in man support the anti-inflammatory action of MSM and a recent study conducted in racehorses reported similar anti-inflammatory and analgesic properties. Recent published research also demonstrated the anti-inflammatory effect of MSM *in vitro* on cultured equine cartilage cells. This work suggests that MSM moderated the production of inflammatory mediators, including certain types of prostaglandins.

Absorption of MSM

Radiolabelling studies have shown MSM to be bioavailable with sulphur derived from MSM being found in blood and a wide range of tissues within 24 hours of administration.

Efficacy

The anti-inflammatory and analgesic effect of MSM in horses has been reported in a placebo-controlled trial in Standardbred racehorses fed 20g of MSM for a period of 6 weeks. Furthermore, *in vitro* work using a pro-inflammatory model based on equine articular cartilage reported that inclusion of MSM in the culture medium reduced the production of the pro-inflammatory mediator PGE₂. There was also a related protective effect of MSM against glycosaminoglycan degradation in this model.

Key Points

- MSM occurs naturally in the horse's diet and provides a bioavailable form of sulphur.
- MSM occurs naturally in the horse's diet, however drying or processing will destroy the majority.
- MSM provides sulphur to repair damaged sulphur-containing bonds such as those found in collagen.
- MSM is a derivative of DMSO and has similar analgesic and anti-inflammatory properties.

❖ Omega-3 fatty acids

Fatty acids are found in high concentrations in oils such as **linseed oil**, **cod liver oil**, **corn oil** and **soya oil**. The position of the first C-C double bond within an unsaturated fatty acid affects its metabolism by the body and this feature is used to further classify unsaturated fatty acids. **Omega-3 fatty acids** are those that have their first C-C double bond between the 3rd and 4th carbon atom counting from the methyl group or omega end. In contrast, **Omega-6 fatty acids** are those that have their first C-C double bond between the 6th and 7th carbon atom counting from the omega end and so forth for Omega-9 fatty acids.

In feed ingredients, **alpha linolenic acid**, which is found in high concentrations in **linseed oil** and **cod liver oil**, is the **major omega-3 fatty acid**; whilst **linoleic**, which is found in high concentrations in **corn** and **soya oil**, is the **major omega-6 fatty acid** and **oleic acid**, which is found in high concentrations in **olive** and many other **vegetable oils**, is the **major omega-9 fatty acid**.

Horses, like man, are unlikely to be able to synthesise fatty acids, which have their first C-C double bond before the 9th carbon atom from the omega end. Thus, omega-3 and omega-6 fatty acids are referred to as essential fatty acids (EFA) as they must be provided by the diet.

Functions of Omega-3 and Omega-6 Fatty Acids

- Involved in many functions within the body including forming parts of vital body structures, forming an integral component of phospholipids (e.g. lung surfactant), blood clotting, involvement in immune function and vision and are integral to all cell membranes.
- Omega-6 fatty acids are converted primarily to **arachadonic acid (pro-inflammatory)**
- Omega-3 fatty acids are converted to **eicosapentanoic acid (EPA)** and **docosahexanoic acid (DHA)** which have **anti-inflammatory** properties.

Omega-3 and omega-6 fatty acids follow different biochemical pathways to produce distinct types of prostoglandins and thromboxanes, each of which have very different effects within the body. The eicosanoids are potent regulators of vital body functions such as blood pressure, blood clotting, immune response and pro-inflammatory responses.

In general terms, the eicosanoids produced from omega 6 fatty acids tend to increase inflammatory processes and blood clotting, whilst those produced from omega-3 fatty acids tend to decrease blood clotting and inflammatory responses, although this is a gross simplification as the mechanisms involved are very complex.

The physical and functional properties of cell membranes are affected by the relative fatty acid composition of membrane bound phospholipids, which can be altered according to the fatty acid composition of dietary triglycerides. The different biochemical pathways involved in eicosanoid production utilise and therefore compete for the same enzymes and so the degree of inflammation, for example, is influenced by the relative proportions of omega-6 and omega-3 fatty acids present in cell membranes.

Evidence for efficacy of dietary Omega-3 fatty acids

The reputed beneficial effects of the omega-3 fatty acids are largely due to the conversion of EPA and DHA to the prostoglandin PG3 series. However, unfortunately the conversion of the parent precursor alpha linolenic acid to both EPA and particularly DHA is relatively inefficient due to low activities of the enzyme delta-6-desaturase. In domestic animals, dietary supplementation with omega-3 fatty acids may be a useful adjunct to treatment in renal disease, rheumatoid arthritis, cutaneous inflammatory disorders, autoimmune disease and possibly cancer. More importantly, as the efficiency of the synthesis of both EPA and DHA is likely to be low, **dietary supplementation with these fatty acids may be of benefit.**

Sources of Omega-3 fatty acids and absorption

Omega 3 fatty acids are found in high concentrations in linseed oil and fish oils, including cod liver and salmon oil. Another potential source of omega-3 fatty acids is the New Zealand green lipped mussel (*Perna canaliculus*). The primary focus of research regarding the use of omega-3 fatty acid supplements for inflammatory joint conditions has until recently been aimed on human rheumatoid arthritis. However a very recent study reported the beneficial effects of omega-3 fatty acids on human osteoarthritis. In addition, several laboratory studies of cartilage-containing cells have found that omega-3 fatty acids decrease inflammation and reduce the activity of enzymes known to be involved in cartilage degradation.

Key Points

- Omega 3 and 6 fatty acids are essential fatty acids (EFA's) and must be provided by the diet.
- The horse's diet is traditionally HIGH in Omega 6 and LOW in Omega-3 fatty acids.
- The main source of Omega-6 fatty acids in the diet is vegetable oil such as corn or soya oil as well as ingredients such as cereals and pulses.
- Omega-6 fatty acids are converted primarily to arachadonic acid which is pro-inflammatory.
- The main source of Omega-3 fatty acids in the horse's diet would be linseed and linseed oil as well as fish oil such as cod liver oil.
- Omega-3 fatty acids are converted to eicosapentanoic acid (EPA) and docosahexanoic acid (DHA) which have anti-inflammatory properties.
- Supplementation with omega-3 fatty acids has been shown to have beneficial effects in human osteoarthritis.

❖ Antioxidants

Reactive oxygen species (ROS) or 'free radicals' are potent mediators of cartilage degradation. An increase in the concentrations of ROS in the synovial fluid of diseased joints (both traumatic arthritis and osteochondrosis) has been reported in comparison to normal joints. ROS are capable of degrading many of the components of the joint including collagen, proteoglycans and hyaluronic acid. The horse has a number of natural defence mechanisms against ROS attack in the form of anti-oxidants. These include enzymes such as superoxide dismutase, glutathione peroxidase and catalase as well as vitamins A, C and E. Ascorbic acid (vitamin C) is required for the normal synthesis of collagen and whilst the horse can synthesise it from glucose in the liver, inflammation may increase the breakdown of both collagen and ascorbic acid.

Other micronutrients normally present in the diet such as copper, manganese and zinc, are also essential co-factors for maintaining healthy cartilage. Copper is required in the production of collagen and also is a co-factor for the enzyme superoxide dismutase. An adequate dietary intake of manganese is required to maintain the concentration and integrity of cartilage proteoglycans. This highlights the need for a balanced and well-fortified diet in addition to any chondroprotective support.

Evaluating Joint Supplements

When choosing a suitable 'joint support' product you may opt for simple but effective glucosamine, or for a more comprehensive combination of ingredients. Whatever your choice, you need to be mindful that these supplements do not always provide the answer and relative success is likely to depend on the injury or disease process in question. Diagnosis by your veterinarian is essential before embarking on nutritional support for an injury or disease situation. However, these chondroprotective supplements are suitable for prophylactic use to offset the increased 'stress' of training and competition. Additionally, whatever the main active ingredient in your supplement of choice, you should be aware of the level of the active ingredient present per daily dose. This will enable you to make valid comparisons between competitive products and to evaluate their relative 'value for money'.

Our domestication of the horse and training for athleticism is likely to have increased its susceptibility to joint problems. An increase in the concussive forces involved in many equestrian sports leaves the horse vulnerable over time. Training, equipment and nutrition should be optimised to reduce the 'stress' imposed on the skeletal system. Of particular relevance to endurance is the ongoing debate over the importance of volume of work versus quality of work in achieving a balance between 'training effects' and 'wear and tear'. A good training and qualification program should strive to minimise the amount of work or 'miles on the clock', whilst still achieving optimum cardiovascular, respiratory, muscular, skeletal and psychological fitness for the task in hand.